

WINTER 2000

# Harvard Medical

ALUMNI BULLETIN



Medical Ethics  
*from conception to death*

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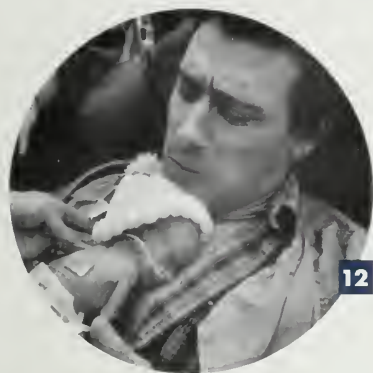
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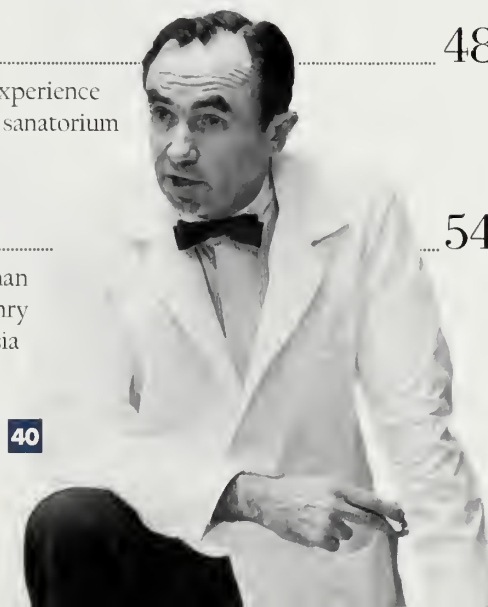
A physician reflects on his experience as a patient in a tuberculosis sanatorium in the 1940s.

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Committed to relieving human suffering, philanthropist Henry Isaiah Dorr gave the anesthesia field an early boost.

*by JOHN P. BUNKER*





## In this Issue

**M**y first attempt to think about ethics came as an assignment when I was a college freshman: to read Kant's *Fundamental Principles of the Metaphysics of Morals*. The book seemed short in my hand but endless on the page. Duty-bound, I read every word with bewildered admiration but no real ability to connect the dots. Since then, I've made sporadic attempts to firm up my grasp of the issues without ever achieving much confidence in the outcome.

Some ethical principles in medicine are comfortably concrete and easily stated: it's never okay to steal from or sleep with your patients. But after you've said that, almost everything else can get surprisingly complicated or subtle. Even "Thou shalt not kill" has proved to be less than straightforward for physicians, because patients counter with, "Whose life is it, anyway?" and say they want us to provide death as a service. The debate over whose life it is becomes poignant in an utterly different way when the person in question is a baby, and competing claims are made by several people who have played one role or another in the child's creation.

It's too easy, and deceptive, to think that ethical uncertainty is driven mainly by advances in technology. Practices that were ordinary even 30 years ago now seem quite alien, primarily because of a remarkable change in our attitudes toward patients' autonomy and their need for information. This change has come about not from advances in scientific medicine, but from a much broader change in concepts of authority and trust in American society as a whole.

Most of the ethical uncertainty that I experience in an average day's work arises from this new, and proper, acknowledgment of the vital role of informed consent. Whether I have truly informed a patient and whether the patient has truly consented proves much more elusive than it would seem to be in the ubiquitous forms now used to "document" the process. Nevertheless, expanding the quest for informed consent can have some marvelous and comforting results, as one of our contributors points out: properly informed and given their choice, some patients will opt to receive less care rather than take it from someone who has a greater need. This is just one row of dots the authors of this issue connect for us as they guide us through some of the complexities of medical ethics today.

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### Balancing Acts

Thank you for the music and medicine issue, which is, to my mind, head and shoulders above anything else the *Bulletin* has ever done.

I have been distributing copies to friends—musicians; premedical advisees, physicians, and nonmedical scientists who are trying to integrate music into their lives; music teachers; performing arts medicine specialists; and others who are trying to lead balanced lives. Your generosity in sending extra copies has saved me from having to commit an illegal act with a photocopier.

Connie Tomaino, who is cited in Samuel Wong's article, has edited a monograph, *Clinical Applications of Music in Neurologic Rehabilitation* (MMB Music, Inc., St. Louis, MO, 1998). The monograph contains a chapter by Oliver Sacks entitled "Music and the Brain."

When I was eight or ten years old, my father brought home a collection of Bach organ works performed by Albert Schweitzer. At the time, I couldn't figure out why on earth a physician would want to be a Bach scholar. Now I know.

JOHN BRAVERMAN LEVINE '79  
CAMBRIDGE, MASSACHUSETTS

*Editor's note:* This year is the 125th anniversary of Albert Schweitzer's birth and the 250th anniversary of J. S. Bach's death—two anniversaries that HMS plans to commemorate in the fall with a single event.

### Food for Thought

Catching up on my reading, I just devoured your summer issue from cover to cover. Many thanks to all the contributors!

RICHARD BAGNALL '43B  
BLOOMFIELD, CONNECTICUT

### The Surgeon and the Composer

I found the summer issue of the *Bulletin* to be fascinating. As a physician working in

internal medicine and hematology, I am very interested in the connections between music and medicine. Among the famous physicians who were also musicians was Theodor Billroth (1829–1894), an outstanding surgeon, pathologist, professor, and mentor at Wien Medical School. Billroth was a close friend of Johannes Brahms, who dedicated his first two string quartets (Opus 51, Nos. 1 and 2) to the famous surgeon. I have presented, several times, a special lecture about their relationship,

showing many pictures and playing selections from Brahms's work.

I want to congratulate you on this very interesting and provocative issue.

ENRIQUE TORRE LÓPEZ, MD  
SAN LUIS POTOSI, MEXICO

### The Beats of Different Drummers

Congratulations on the publication of the summer issue. It articulated and amplified a subject in which I have been interested for the past 25 years. Music has been used for healing since early times, yet its study is neglected today.

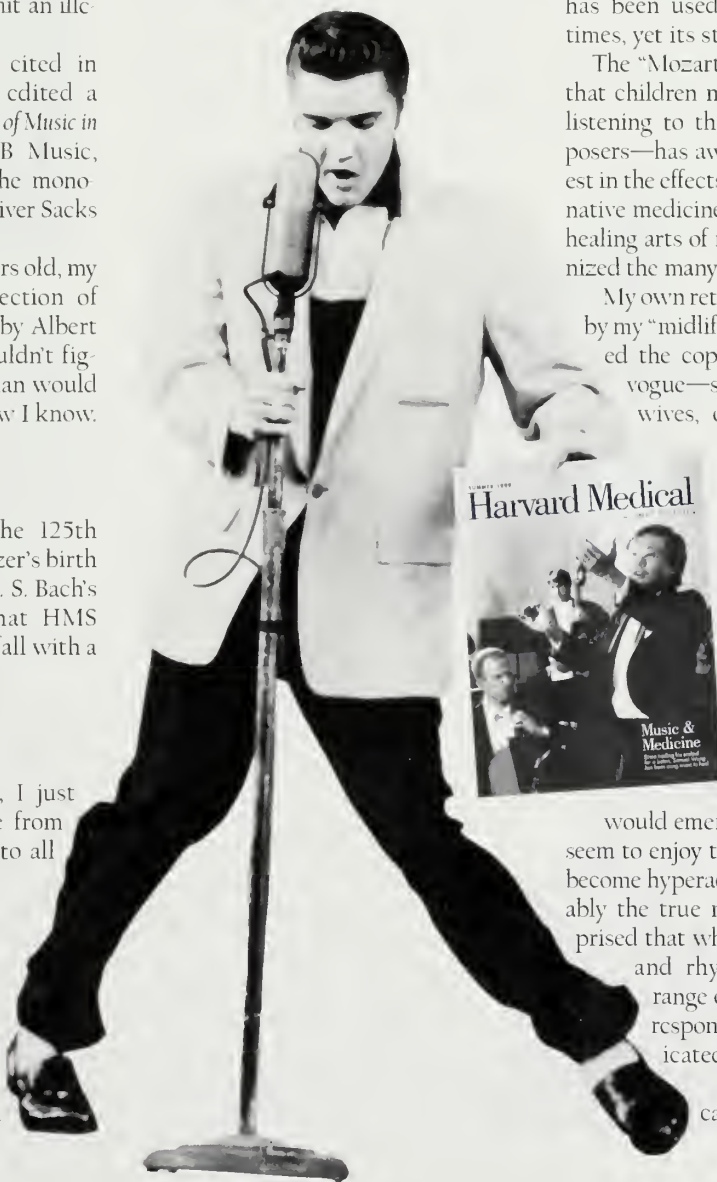
The "Mozart effect"—which suggests that children may increase their IQs by listening to the music of certain composers—has awakened a renewed interest in the effects of music. For cons, alternative medicine, which incorporates the healing arts of many cultures, has recognized the many depths of healing.

My own return to music was sparked by my "midlife crisis," in which I rejected the coping mechanisms then in vogue—such as jogging, changing wives, or wallowing in narcissism—and turned to popular music, rather than the classical genre in which I was raised.

At the time, my mother was in a nursing home with severe Alzheimer's disease. I would play the piano for her and her fellow residents, evoking many mixed reactions. Some medicated patients

would emerge from their stupor and seem to enjoy the sounds. Others would become hyperactive and outraged (probably the true music lovers). I was surprised that when I varied the tonalities and rhythms, I would elicit a range of emotional and physical responses, even in heavily medicated patients.

Were their responses caused by conditioning or





the actual sounds? After all, I was playing ragtime and jazz—the “brothel music” of their early days. Were their responses physical? Cultural? Did they involve aesthetic judgment? One woman became overtly hostile to my playing, but when I switched to a folk song of her culture, she became docile.

The most interesting case was a man with catatonic schizophrenia who was taken to a porch where a jazz band was playing. At the first notes, he became responsive and remained so until the music stopped, at which time he resumed rigid catatonia.

At our 45th reunion, when Dr. Gerald Fischbach's group presented newer work in neurobiology, one of the lecturers spoke about cocaine addiction. He stated that recovered cocaine addicts might relapse if exposed to the music they had heard while in the drug culture. Apparently such a relapse is not the case with hero-

in, marijuana, or other addictive substances. I asked if anyone had tried to use music as a desensitizing agent. As I recall, no one had.

I found the responses of surgeons and anesthesiologists to the playing of music in the operating room to be fascinating. But I wonder if doctors shouldn't be careful, because their patients' reactions to music in the O.R. might influence postoperative results. I would hesitate to guess what my own vital signs would do if the “wrong” music were played while I was anesthetized. These observations certainly warrant study.

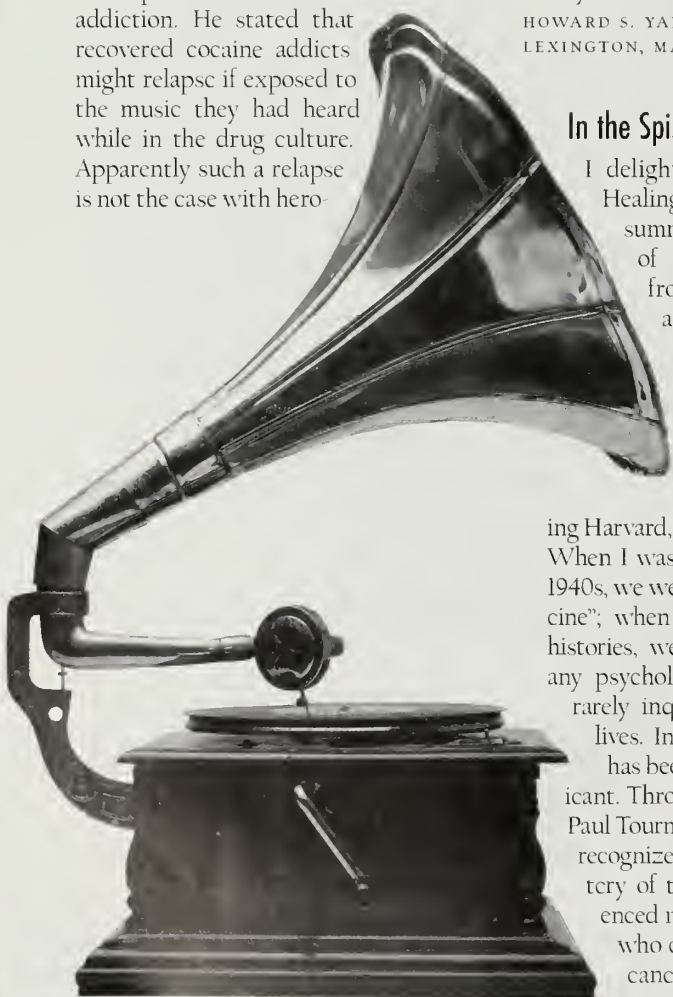
Again, congratulations to all hands for producing a groundbreaking issue. I think the watchwords should be, “everyone has his own song.”

HOWARD S. YAFFEE '51  
LEXINGTON, MASSACHUSETTS

### In the Spirit of Healing

I delighted in reading “Musical Healing” by Samuel Wong in the summer issue. Despite the lack of universal improvement from music therapy, as alleged by Christopher Chabris, the anecdotes that Dr. Wong describes so vividly are impressive.

I understand that most of our early American universities, including Harvard, were begun by Christians. When I was a medical student in the 1940s, we were taught “scientific medicine”; when taking patients' medical histories, we were careful to include any psychological manifestations yet rarely inquired into their spiritual lives. In recent times, spirituality has been shown to be very significant. Through his personal faith, Dr. Paul Tournier of Switzerland came to recognize what he called the “mystery of the person,” and he influenced many European physicians, who came to realize the significance of spirituality in disease.



### Cerebral

*Symphony*

How do the miniature orchestras in our brains translate music?  
by DEBRA MALINA



Harvard's own Dr. Herbert Benson was one of the first in this country to perform careful medical research on the physiological effects of meditation. He showed that lower blood pressure, a slower heart rate, and a lower metabolic rate could be achieved. In his book *Wired for God*, he claimed to have “found that in every nation, in every religion, the results were the same...there was transforming power in prayer.”

Scientific controlled studies have since corroborated this statement. Dr. Larry Dossey has written in *Healing Words* that he decided—after a thorough search of the literature regarding spiritual influences on healing—that not to employ prayer with his patients was the equivalent of “deliberately withholding a potent drug or surgical procedure.”

The medical schools at Harvard, Yale, Dartmouth, Johns Hopkins, and many other universities recognize benefits from prayer, personal faith, church attendance, and meditation. I have a bright 16 year old grandchild who, at age of six months, was cured by prayer



of a highly malignant brain tumor that had been confirmed by pathologic study.

Dr. Paul Brand, surgeon, missionary to lepers in India, and author of *Fearfully and Wonderfully Made*, has taught that four states affect pain and our immune systems:

*Persistent anger makes worse, and forgiveness better*  
*Fear makes worse, and peace and reassurance better*  
*Loneliness makes worse, and visitation better*  
*Inactivity makes worse, and activity better*

Health providers, friends, and our own lifestyles can significantly benefit from these considerations. Dr. Wong is to be congratulated for bringing "Musical Healing" to our attention.

ISAAC V. MANLY '46  
 RALEIGH, NORTH CAROLINA

## Musician, Heal Thyself

In your fascinating issue on music and medicine, you missed the Longwood

Symphony Orchestra—"the orchestra of Boston's Medical Community." Many HMS faculty physicians, students, post-docs, and alumnae/i contribute to some of the sweetest sounds at New England Conservatory's Jordan Hall, where concerts benefit cancer research, student medical mentoring programs, birth defect and substance abuse prevention programs, etc. When Yo-Yo Ma played with the Longwood Symphony in the Schweitzer Reverence for Life Concert, his benefit performance was conditioned upon free tickets for homeless people. The Longwood Symphony has played at HMS for the Urban Health Project and at the Harvard Club for the Aesculapian Society.

The Longwood Symphony; its president, Lisa Wong, a pediatrician at Massachusetts General Hospital; and Musical Director Francisco Noya provide a fine opportunity for physicians to "heal themselves" while serving the broad HMS community.

SUSAN P. PAUKER, MD  
 BOSTON, MASSACHUSETTS

*Editor's note:* The connections between music and medicine are very rich, especially at HMS. We greatly regret the fact that space constraints kept us from profiling the Longwood Symphony Orchestra, the Harvard Medical School Music Society, and all of the many alumni who are gifted musical performers.

## Striking the Right Chord

Congratulations on your music and medicine issue! I've been involved with numerous publications covering this topic, and none has done it as well as you and your staff. A number of colleagues have asked for copies of the issue.

MARK JUDE TRAMO, MD, PHD  
 BOSTON, MASSACHUSETTS

*Editor's note:* Dr. Tramo pointed out an error in the article that featured his work: in the last paragraph of page 26, "medulla oblongata" should have been "amygdala." We regret the error.

## The Sound of Music

The summer issue of the *Bulletin* resonated with special, fond memories of how music mixed with medicine during my HMS years from 1971 to 1975. Indeed, Vanderbilt Hall seemed to be a muse for many of us. Along with three other students, I was drawn to the courtyard's natural acoustics as an ideal venue for Christmas carols by an impromptu brass quartet. A few serious students objected to our disturbing the silence, but many more welcomed the brief diversion and engagement with the spirit of the season. Assuming that the acoustics have not changed in the intervening decades, and as long as the public peace is not unduly disturbed, I highly recommend the courtyard for chamber music performance.

BRUCE BARNETT '75  
 ENCINO, CALIFORNIA

*The Bulletin welcomes letters to the editor. Please send letters by mail (Harvard Medical Alumni Bulletin, 25 Shattuck Street, Boston, Massachusetts 02115); fax (617 432-0013); or email (bulletin@hms.harvard.edu). Letters may be edited for length or clarity.*





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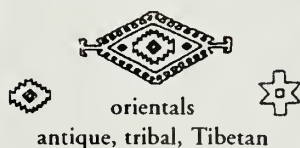
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## President's Report



THE FALL MEETING OF

the Alumni Council, which was held October 28 and 29, marked the beginning of a special year celebrating "Harvard Medicine at the Millennium."

Serious planning for the year ahead had actually begun last June during Alumni Week, when former Council President George Thibault '69 and I discussed the possibility of greater coordination and year-to-year continuity in planning Alumni Council affairs. To this end, before the fall meeting, the newly formed Alumni Council Executive Committee, also known as the Presidents' Group—consisting of George Thibault, the next two presidents-elect (Charles Hatem '66 and Paul Davis '63), and me—met with Daniel Federman '53, director of alumni relations, and Nora Nerecessian, assistant dean for alumni affairs and special projects, to set future priorities for the Council.

At the fall meeting, the Council discussed special programs to mark the millennium. We also heard an update on events already scheduled for the coming year. Highlights include a number of invited lecturers; research symposia, including a public event on the subject of "Brain Science at the Millennium"; and a major retreat on the topic of "Clinical Education for the New Millennium," which will deal with the challenges of integrating informatics, technology, genomics, and social issues into the curriculum.

Council members then reviewed the School's finances and the role of alumni giving in maintaining the financial health of HMS and its students. Leading these discussions were Paul Levy, executive dean for administration; Mary Campion, dean for resources; and Tenley Albright '61,

chair of the Alumni Fund. Although it represents only a small percentage of the overall HMS budget, alumni giving is clearly an important component of student scholarship support and the dean's discretionary funds.

The Council considered reconstituting its Alumni Survey Committee (which has been inactive in recent years) in order to survey HMS alumni at the millennium. The last survey was conducted a decade ago, and the concept of taking a snapshot of what our alumni are doing and thinking at the turn of the century held great appeal for Council members. The survey results would likely be of considerable interest, meriting dissemination not just within the HMS family, but also to the public. Time did not permit us to finalize planning for the survey. Alumni volunteers interested in working on it should contact me.

The rest of our meeting was consumed with planning an Alumni Council/Town Meeting to be held in Washington, DC on March 17 and 18. The decision to take the Alumni Council "on the road" and involve locally prominent alumni in the event is the Council's effort to engage alumni from around the country. We hope to start a national dialogue about issues of concern to alumni, about either HMS or their professional lives.

As always, the Council members welcome your views, as our goals are to present alumni opinions and recommendations to the administration and faculty of HMS, and to promote alumni interests and fellowship. Feel free to contact Dan, Nora, or me through the Office of Alumni Affairs (phone: 617 432-1560; email: alumni\_council@hms.harvard.edu). ■

*Sharon B. Murphy '69 is chief of the Division of Hematology/Oncology at Children's Memorial Hospital in Chicago.*



## New Cancer Center Launched

**H**MS IS JOINING WITH FIVE OF its affiliated hospitals and the Harvard School of Public Health to fight cancer. The combined effort, the largest private cancer-research initiative in the United States, has taken the name Dana Farber/Harvard Cancer Center (DF/HCC). The collaborators, which conduct more than \$235 million in cancer-related research each year, include Dana-Farber Cancer Institute, Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Children's Hospital, and Massachusetts General Hospital.

"One primary goal for this center is to take advantage of current trends in biomedical science that focus upon multidisciplinary research to yield exciting new advances," said HMS Dean Joseph Martin. "The new center is already creating this research synergy because we know researchers have found each other through its programs who would not have through our old system."

"All of the DF/HCC member institutions conduct incredible basic, clinical, and population-based research," said Dana-Farber President David Nathan. "Now we will have the mechanisms to knit these efforts together to share resources and coordinate our efforts in a more focused and efficient manner."

Martin and Nathan initiated discussions about the collaboration more than two years ago. By the spring of 1999, more than 800 Harvard faculty based at the various institutions had signed on as center members. More than half of those researchers have already begun collaborations. Activities under the DF/HCC banner will

occupy nearly 500,000 square feet of space at the institute.

The institutions have already committed significant funds to create or enhance more than a dozen core facilities—ranging from DNA sequencing operations to pathology laboratories—which will be available to all members. These core facilities tend to be large, highly instrumented laboratories that are too expensive for any one researcher, or often any one institution, to initiate. Other core facilities provide non-laboratory services, such as health communication to high-risk populations.

The initial phase of the DF/HCC has created disease-based programs for five types of cancer: breast, gynecologic, leukemia, lymphoma, and prostate. As these programs move forward, the center will be developing collaborative programs for seven other types of cancer: brain, gas-

trointestinal, head and neck, skin, soft tissue sarcomas, lung, and AIDS related malignancies.

The five existing disease-based programs are designed to interact with ten discipline-based programs: biostatistics, cancer cell biology, cancer genetics, cancer immunology, viral oncology, cancer epidemiology, risk reduction, outcomes research, cancer imaging, and experimental therapeutics. Another nine discipline-based programs are envisioned for development over the next few years.

Its founders hope the center's structure will enable researchers from all disciplines to synthesize the vast amount of information generated by individual studies. They also hope it will speed researchers' efforts to develop new intervention strategies. ■



**TEAMING UP AGAINST CANCER:** David Nathan (left) and Joseph Martin join forces

## Shifts in Medical Education Leadership

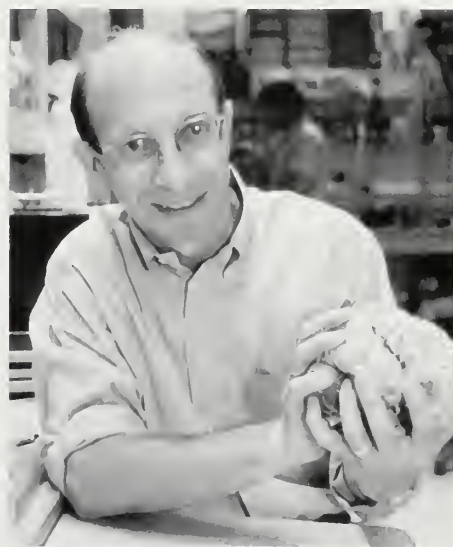
DANIEL LOWENSTEIN '83, A NEUROLOGIST AT the University of California, San Francisco (UCSF), will become the new HMS dean for medical education on July 1. He will succeed Daniel Federman '53, whose administrative career at HMS has spanned two decades.

Lowenstein is currently professor of neurology, otology, and neurosurgery at UCSF. He directs the Epilepsy Research Laboratory and attends at San Francisco General Hospital. In 1998, he won the prestigious Alpha Omega Alpha Robert J. Glaser Distinguished Teacher Award from the Association of American Medical Colleges.

"We are indeed fortunate to have Don Lowenstein come back to Harvard," says Dean Joseph Martin, who worked with Lowenstein as chancellor of UCSF. "He is the quintessential educator, a great favorite of the students, and a fine physician-scientist."

"I am thrilled that we have been able to get Don Lowenstein to return to HMS," Federman adds. "There has

continued on page 8



**RARING TO GET STARTED:** Daniel Lowenstein will become the new dean for medical education in July.

## Medical Education Leadership (continued from page 7)

never been a more promising—and simultaneously more challenging—time in medicine, in science, and in their social setting. Don has shown outstanding accomplishment across that whole spectrum, and our students, faculty, educators, and staff are all fortunate to have a new leader of his caliber.”

Lowenstein, in turn, lauds Federmon’s legacy. “The prospect of following in the footsteps of Don Federmon is both humbling and daunting, but I am delighted to enter into this role as a beneficiary of his great leadership,” he says. “My visits to Boston over the past few months, offering away for so long, have been pleasant reminders of the extraordinary qualities of the people here at HMS. I look forward to renewing many old friendships and establishing new ones, and I am raring to get started.”

Lowenstein’s basic scientific research focuses on the molecular and cellular changes in neural networks following seizures. He and his colleagues developed animal models to study responses to seizures and have identified changes in the expression of a variety of genes.

Federmon is not so much stepping down as stepping aside. In September, Martin appointed him as senior dean for alumni relations and clinical teaching, a position in which he will work with alumni to increase scholarship funds and help conduct a review of the third- and fourth-year curriculum.

Federmon served on the School’s faculty from 1960 to 1972. Following a five-year stint at the Stanford University School of Medicine, he returned to HMS as dean for students and alumni and, since 1989, dean for medical education. ■

## Building D Gets a New Name

**S**TONE MASONS RECENTLY FINISHED CARVING A NEW NAME INTO THE exterior of Building D in honor of a generous benefactor. The new name will be the Count Giovanni Auletta Armenise Medical Research Building.

The Giovanni Armenise-Harvard Foundation was established in 1997 to nurture research and education in cellular and molecular biology, and to foster collaboration between researchers at HMS and those in Italy. The foundation supports the exploration of fundamental questions in biology based on the conviction that such discoveries will lead to significant advances in health care and agriculture.

The foundation has funded four new Centers for Advanced Scientific Research at Harvard, as well as new programs at five selected centers of scientific excellence in Italy, with the intent of pairing scientists and laboratories to encourage intellectual exchange and collaboration.

Armenise’s interest in HMS began when his wife, Dianora Bertacchini, was treated at Massachusetts General Hospital for a brain tumor. They both believed that the answers to questions posed by her illness lay in basic research, and they agreed on the concept of starting a research foundation before her death in 1994. ■



## New Clinical Exam

**L**AST SUMMER, FOR THE FIRST time, all fourth year HMS students took a standardized, comprehensive clinical examination. Although HMS students have received extensive clinical training by their fourth year, this was the first such exam the students have taken as a class.

Developed as an annual event based on the objective structured clinical exam (OSCE) format, the evaluation was established for several reasons. The National



**REACHING OUT:** As part of the School’s Global Harmony/Ebert Community Service Day festivities on October 7, Sheela Rao ’01 performed a classical Indian dance.





**TESTING TECHNIQUES:** Last summer, for the first time, fourth-year HMS students took a standardized clinical exam.

patient roles, and give feedback. The other three had materials to be interpreted, such as lab results or x-rays.

The skills that were tested included history taking, physical examination, differential diagnosis, patient education, test interpretation, clinical reasoning, and treatment planning. At the end of each session, the examiners and standardized patients evaluated the student's performance and gave feedback.

The exam was well received by the OSCE participants—faculty and students alike. Valerie Pronio Stelluto, a faculty examiner, said, "It is a pleasure to see these bright students evolve into young physicians." Typical comments from faculty examiners on evaluation forms included: "A wonderful experience for examiner and student."

Fourth-year students seemed to enjoy the exam, too. "This was fantastic," one student wrote. "Feedback was so helpful." For many, it was a confidence builder. Said another student: "Even though I dreaded taking this, I found it to be a productive exercise and actually enjoyed it." ■

## HMS at the Millennium

**D** EAN JOSEPH MARTIN IS MARKING the new millennium with a series of events that highlight past advances and future opportunities in medicine. HMS has worked with the Harvard School of Dental Medicine to design the program, entitled "On the Threshold—Harvard Medicine at the Millennium." Events explore issues ranging from brain science and research trends in aging to information technology in the New Pathway. For details, visit the Web site at [www.hms.harvard.edu/OnTheThreshold/index.html](http://www.hms.harvard.edu/OnTheThreshold/index.html). ■

## SAVE THE DATES

### Alumni Events to Mark the Millennium

What progress are we making in gene therapy? What new imaging techniques are being used? What is computational genetics? To update alumni about clinical advances, research accomplishments, and proposed programs, the Harvard Medical Alumni Council will host a two-part seminar at the Quadrangle. "HMS at the Millennium: What's New and What's Happening in and around the Quadrangle" will take place on October 20 from 3:00 to 5:30 p.m. and October 21 from 10:00 a.m. to 12:30 p.m. CME Category 1 credit will be available.

For more information, call Tenley Albright '61 at 617-247-8202, or email her at [Tenley1003@aol.com](mailto:Tenley1003@aol.com).



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## New Fronts in Attention Deficit Hyperactivity Disorder

**R**ESearch ON ATTENTION DEFICIT hyperactivity disorder (ADHD) has been fraught with controversy lately. Are too many children incorrectly diagnosed with ADHD? Are children with the disorder overmedicated? Can stimulants lead adolescents with ADHD to abuse their prescriptions or take street drugs?

HMS researchers have made important strides on the ADHD front in the past year, says Timothy Wilens, associate professor of psychiatry at Massachusetts General Hospital (MGH). These advances include studies on novel treatments, a budding effort to develop a biologically based diagnosis for the disorder, and early research on possible genetic components of the disease.

ADHD is the most common cognitive, emotional, and behavioral disorder treated in children. About 25 epidemiological studies in different countries estimate that it affects approximately 4 percent of children and adolescents. Medication, mostly with stimulant drugs and tricyclic antidepressants, is a mainstay of ADHD treatment, along with psychotherapy and behavior modification.

One misperception, says Wilens, is that ADHD is overtreated. Fueling this concern are isolated cases, such as a well-publicized study in September 1999 that found that almost 20 percent of white male fifth-graders in one Virginia district were on medication. From a public health perspective, however, Wilens believes that ADHD remains undertreated, especially in light of recent data shoring up the usefulness of drug therapy. For instance, he explains, Massachusetts Medicaid records indicate that less than 1 percent of children in that program receive ADHD medication.

Along with Joseph Biederman, HMS professor of psychiatry, and other researchers in the MGH Pediatric Psychopharmacology Unit, Wilens is studying the effects of many psychi-

atric drugs in children, adolescents, and adults. In December 1999, Wilens and his colleagues described in the *American Journal of Psychiatry* the initial results of a clinical trial of a new class of drugs to treat ADHD. Although the biological cause of ADHD remains unclear, most research points to insufficient norepinephrine and dopamine activity in the frontal cortex and striatum areas of the brain. Indeed, most medications used for ADHD target dopamine and norepinephrine.

The new drug (ABT-418) doesn't target dopamine, but instead acts through a different path of the brain's chemistry. Developed by Abbott Laboratories, which supported the MGH researchers,

it is a chemical relative of nicotine. Touted as a kind of "designer nicotine," it stimulates attention without exerting nicotine's dangerous effects. Wilens says the compound intrigued him because it has been found that teenagers and adults with ADHD smoke at twice the rate of the general population.

Wilens and his colleagues at MGH tested the compound in 29 adults with ADHD in a double-blind, placebo-controlled trial. After six weeks, 40 percent of those receiving the test substance and 13 percent of those on placebo were "much" or "very much" improved. The compound worked preferentially better on the attentional symptoms of ADHD compared to the hyperactivity or impulsivity.

Scientifically, this compound breaks new ground. Broadly speaking, the brain has two major neurotransmitter



**STRAIGHT TALK:** Timothy Wilens recently wrote a book to help parents sort through the agonizing pros and cons of putting their children on psychoactive drugs.

systems relevant to ADHD: the catecholaminergic system, which includes dopamine, and the cholinergic system, in which so-called nicotinic receptors are one of two major recipients of the neurotransmitter acetylcholine. Nicotine binds these receptors, as does the new compound. The drug is presumed to mediate between the two systems.

"This is one of the first times that a cholinergic agent proved in a clinical trial to be effective for ADHD," says Wilens. "This new class of agent is worth investigating in larger studies, because it helps with some of the symptoms that do not respond well to the standard ADHD medications."

Even if larger studies confirm these results, it remains to be seen whether the findings will have any implications for ADHD in children. Wilens believes they will, explaining that he and his colleagues have extensive new data showing that people with ADHD have consistent responses to medications throughout their lives.

This consistency touches on another controversial point—ADHD among adults. "The drug responsiveness data is further evidence," Wilens says, "that whatever brain defect we are talking about in children really does continue into adulthood."

### The Promise of Objective Diagnoses

Do you ever fail to pay close attention to details? Have difficulty organizing tasks? Lose things? Interrupt others? Although these are some of the ADHD symptoms listed in the diagnostic manual DSM-IV, admitting to these failings probably does not mean you have the disorder. And these examples suggest just how easily local pockets of over-diagnosis can occur.

"We would love to have a biologically based diagnosis," says Wilens. He may soon get his wish. In a research letter published in *The Lancet* in December 1999, Harvard scientists describe a potential tool to reveal ADHD—an

imaging method they developed to diagnose Parkinson's disease.

Alan Fischman, associate professor of radiology at MGH, worked with Bertha Madras, professor of psychobiology in the Department of Psychiatry at the New England Regional Primate Research Center, to test a SPECT imaging agent that can detect and quantify in a person's brain a protein called the dopamine transporter. This transporter can do diagnostic double-duty because it vanishes as dopamine neurons die in Parkinson's, yet is elevated in people with ADHD. The transporter is already the target for the drug methylphenidate (Ritalin) and has been implicated as a cause of ADHD.

This initial trial included only six adults with previously diagnosed ADHD. The results, however, were clear. All six had dopamine transporter levels in their striatum that were roughly 70 percent higher than controls, and there was no overlap between cases and controls.

Further trials are being planned, says Madras, adding that, even if all goes well, the test will not be brought to the market for several years.

### Jury Still Out on ADHD Genes

Four scientific groups have independently implicated the dopamine receptor 4 gene in ADHD. In May 1999, Steven Faraone, HMS associate professor of psychology, and researchers in the MGH Pediatric Psychopharmacology Unit described in the *American Journal of Psychiatry* how they found that the presence of a certain allele of this gene predicted the disorder in 27 triads of an ADHD adult, his or her spouse, and an affected child.



**THROUGH THE AGES:** Researchers are studying the effects of psychiatric drugs in children, adolescents, and adults with attention deficit hyperactivity disorder.

Intriguingly, in 1998, researchers in Arizona cast suspicion on a polymorphism of the dopamine transporter, a channel that removes excess transmitter from the synaptic cleft. Fischman and Madras have imaged this protein in their diagnostic study.

It is important to remember, however, that in psychiatry many attempts to link genes to diseases have subsequently been refuted. Alcoholism and schizophrenia are just two examples of diseases for which genetic links could not be confirmed. And in this case, too, researchers at other institutions have reported that they cannot replicate the dopamine receptor connection.

Most ADHD research occurs amid controversy, so it is fair to assume that passionate debate will continue as more data on the genetics of ADHD emerge. ■

*Gabrielle Strobel is a science writer for Focus.*



# small WONDERS

**Dramatic breakthroughs in reproductive technology are creating miracle babies—and raising tough ethical issues**

AFTER A YEAR OF UNSUCCESSFUL ATTEMPTS AT PREGNANCY, a miscarriage, and months of infertility treatment, Maureen Connelly suddenly found herself “too pregnant.”

Connelly, then 34 and diagnosed with endometriosis, had produced seven embryos from prior procedures with her husband, Jeffrey Krane, using in vitro fertilization (IVF).

Six of their frozen embryos survived the thawing process, and they had them all implanted, both “by choice and by ignorance,” Connelly says. “There was a lower chance of pregnancy with frozen embryos. Also, we incorrectly thought they all had to be thawed simultaneously. Because we were physicians ourselves, I think certain assumptions were made about our knowledge.”

When the technician performed the ultrasound six weeks later, he looked at the couple. “Are you ready for

*by* PHYLLIS L. FAGELL





**EARLY ARRIVAL:** Erica cradles her newborn son, Harry, who was born ten weeks early weighing only one pound, seven ounces.

“In 1980, donor insemination for a single woman was an issue we deal with now. In ten years we’ll be wrestling with

three?” he asked. Within an hour, they met with a genetic counselor to discuss the implications of having triplets and the pros and cons of multifetal pregnancy reduction.

With existing and emerging assisted reproductive technologies (ART) changing the landscape of fertility medicine, patients like Connelly must navigate a maze of treatments with acronyms like GIFT, ZIFT, ICSI, MESA, and TESE, treatments that have collectively led to the births of more than 70,000 babies in the United States. At the same time, professionals working in the field—including reproductive endocrinologists, urologists, obstetricians, neonatologists, mental health clinicians, scientists, nurses, and ethicists—are grappling with increasingly complex ethical questions.

“Those we met with believed a twin pregnancy would be better for the babies and for me,” Connelly says. “But they told us that 95 percent of triplets were healthy. We liked the odds. Then we saw an ultrasound at ten weeks and saw all three babies moving. That eliminated the possibility of selective reduction for me.”

Unfortunately, by 18 weeks Connelly knew one baby was developing more slowly than the others. Her son Joshua “basically starved for oxygen in the uterus,” she says. He was born at 35 weeks with autism and cerebral palsy. The other two, a boy and a girl, are healthy.

“Joshua is very disabled,” Connelly says. “When we took him home, we could see he was developing differently. He resisted being cuddled and had trouble making eye contact.”

Despite the challenges, Connelly says she wouldn’t trade her situation for anything. “We have a beautiful outcome.”

### Not a Static Field

In a waiting room at Boston IVF, patients seeking infertility treatment

wait to be called. On any given day, these patients may include a woman with breast cancer who wants to postpone chemotherapy in order to take fertility drugs and freeze embryos, a lesbian who wants to use a gay friend’s sperm to conceive a baby, or a couple that wants an egg only from a donor who can give them an “Ivy League baby.”

As the technologies help increasing numbers of infertile couples, their care providers are struggling with difficult questions about the definitions of identity and family, and about what constitutes good, responsible health care.

“Assisted reproduction is not a static field,” says Robert Barbieri ’77, chairman of the department of obstetrics and gynecology at Brigham and Women’s Hospital. “In 1980, donor insemination for a single woman was an ethical dilemma for many clinicians, but that is simple compared to issues we deal with now. In ten years we’ll be wrestling with new ethical dilemmas, probably some we can barely imagine today.”

Kenneth Ryan ’52, chairman of the ethics committee of the American Society of Reproductive Medicine and a professor emeritus at HMS, underscores how quickly the field has been evolving.

“When I started practicing infertility medicine in the 1950s,” he says, “our major tool was a thermometer to chart the woman’s monthly temperature curve. We measured sperm counts and evaluated sperm survival on the cervix. We had no fertility drugs, no way of correcting anovulation.”

Through all the advances in reproductive technology, the object has remained the same, says R. Douglas Powers, scientific and laboratory director at Boston IVF and a lecturer at HMS. “The goal is to get one perfect egg from a woman that leads to one embryo that develops into one healthy baby.”

But currently, he explains, “most programs worldwide will transfer two

or three embryos to a woman. We don’t know whether all three or none will implant, and sometimes all three do.”

### Life and Death in the NICU

Neonatal intensive care units (NICUs) have felt the impact of the new technologies. The risk of prematurity with multiple births translates into a heightened risk that the babies will have to be admitted to the NICU. “We’ve seen a





ethical dilemma for many clinicians, but that is simple compared new ethical dilemmas, probably some we can barely imagine today.”



dramatic increase in multiple births from reproductive technology,” says Steven Ringer, director of newborn medicine at Brigham and Women’s Hospital. “Each year we deliver about 15 sets of triplets, 90 percent of whom are products of reproductive technologies. And about half the twins we see are the result of these technologies.”

If one baby in a multiple pregnancy is at risk, deciding when to deliver can pose a quandary for care providers,

Ringer says. “You can’t take one baby out and leave the others in. The dilemma becomes, is there a time when it’s safer to deliver all three? Do you hope the sick one does better? Or do you expose the healthy siblings to all the risks of prematurity?”

Although life and death issues have always been difficult in the NICU, ART and advances in care have complicated matters. “In the past, it was unlikely that you could save the baby’s life in the

first place,” Ringer says. “That is rarely the issue now. Now it’s more a question of saving babies, but in doing so, condemning them to a miserable life. I can remember telling one set of parents that their child had a 95 percent chance of having terrible cerebral palsy and mental retardation, but I wasn’t at the point of telling them to terminate care. I’m not sure I did the right thing.”

### Emerging Technology

Now, just five years after Connelly underwent infertility treatment, a relatively new technique holds promise for helping women using ART avoid high-order multiple births.

“Normally embryos are transferred the third day after IVF, at the eight-cell stage,” Powcrs says. “Yet some of the embryos naturally stop growing between days three and five. So it’s possible on day five, when embryos in the laboratory turn into blastocysts, to select embryos with a higher probability of implanting. We only transfer two blastocysts to a patient. The pregnancy rates are just as high as with the day-three embryo transfers, but so far we have never had a triplet pregnancy.

“Ultimately, I think we’ll transfer at the blastocyst stage every time,” Powcrs adds. “The challenge has been that an embryo’s metabolic requirements change from day three to day five. It’s only in the last two years that we’ve been able to develop good culture media to make it possible.”

With fewer high-order multiple births, there will be less prematurity, but blastocyst technology is not yet as reliable as it needs to be, Ringer says. “With improvement of the technique,” he adds, “the practice of putting in four embryos with the hope that one will take will not be as necessary. We would welcome the tremendous impact that would have on the NICU.”



“Are we being idealistic in wishing people would be motivated young woman for her eggs, and she sees it as her way to buy a

### Using Donor Eggs

Success rates for IVF drop significantly as women age, says Sharon Steinberg, a mental health clinical nurse specialist in the Center for Fertility and Reproductive Health at Harvard Vanguard Medical Associates. “The media mistakenly perpetuate the belief that IVF works for everyone,” she says. “For women with premature ovarian failure or for whom IVF has failed, use of a donor egg may be presented as an alternative treatment.”

The process involves retrieving an egg from a donor, fertilizing it with the recipient’s partner’s sperm, and transferring the resulting embryo to the recipient. But bringing a third party into the reproductive equation poses significant ethical questions for everyone involved, Steinberg adds. “It’s an unusual relationship between the donor and the physician, because the physician is caring for the recipient and the donor is often paid. We need more dialogue on a national or policy level about the appropriate use of this technology. We also need a registry of how many children are produced from donor eggs, like the kind we keep for donor sperm.”

“Donor eggs offer an attractive alternative to couples when the woman has diminished ovarian reserve,” says Natalie Schultz, a reproductive endocrinologist at Harvard Vanguard Medical Associates. “The infertile woman experiences pregnancy, and the father is the genetic father.

“My concern is the industrialization of this treatment,” she adds. “The financial incentives can be quite seductive to some young women. It would be ideal if a disinterested third party educated donors to ensure that they are giving fully informed consent. For some women, it may be difficult to grasp the future ramifications when the immediate incentives are so tangible. It’s impor-



tant for donors to understand that their fertility may be compromised, and that there have been no long-term follow-up studies on the psychological, medical, and fertility status of these women.”

### The Role of Health Care Providers

“It’s troubling to use the word ‘donor,’ given the thousands of dollars that a couple may pay a woman for going through this process and giving her ovum,” says Jeane Ungerleider-Springer, director of psychological services at Boston IVF. “Yet are we, as health care providers, being idealistic in wishing people would be motivated for altruistic reasons? When a couple offers \$50,000 to a young woman for her eggs, and she sees it as her way to buy a condominium, are we to decide she shouldn’t be a donor?”

Ungerleider-Springer tries to sort out what such arrangements mean to everyone involved, including the donor and the eventual child. “It’s important that the mental health provider in reproductive medicine have a voice,” she says. “I present my assessment and make recommendations as one member of the caregiver team.”

Schultz supports her patients’ decisions, but tries to help couples understand any issues that may not be readily apparent. For example, she explains, “with egg donation, you can create 20, 30, 40 half siblings, and it eventually may be possible for these siblings to search.

“I believe insurance should cover adoption,” she adds. “People might be happy to adopt, but since Massachusetts insurance pays for egg donation, there’s a huge financial incentive to pursue this technology.”

# for altruistic reasons? When a couple offers \$50,000 to a condominium, are we to decide she shouldn't be a donor?"

With adoption, Schultz explains, "there's an agency that advocates for the baby and birth mother. With donor gametes, there is no advocate or follow-up of the donors or offspring. No one knows what it means for a child to have a 63 year-old mother, or to be told he has half-siblings, or to find out that the genetic mother was paid \$6,000 for her eggs. The sale of blood and organs has been outlawed in every other field of medicine. It is unclear why eggs should be available as a consumer commodity."

Consanguinity is another one of her concerns. "You can't freeze eggs, so the gametes can't be stored and shipped around the country as with sperm banks," Schultz says. "The children are all born locally," she adds, relating the story of an IVF nurse who watched two children, offspring of the same egg donor, playing together in a playground. The parents had no idea the children were half siblings.

"There is no registry of how many times a woman has cycled, and of how many babies are born immediately and later with stored frozen embryos," Schultz adds. "I'm not against the use of egg donation. I'm against the abuse. It is a good treatment, but like all treatments, it should be used judiciously."

Diane,\* a 46-year old mother of a three-year old girl conceived using a donor egg, did not care if her donor was motivated by money.

"My biggest concern, other than weeding out those with physical diseases, was how comfortable the donor would be if my baby sought her out," Diane says. "She was 27 at the time and had two children. As another working mother, I could appreciate her wanting to donate both to earn money and to share."

Diane, who chose egg donation over adoption because her insurance covered the procedure, did have other concerns. "At times I felt my husband and I should use donor sperm as well," she

confesses. "I wanted some even ground, for the baby to be genetically related to neither of us." She also worries about the future, when her "already bull-headed" daughter confronts her. "I imagine we'll have fights, and she'll say, 'You're not my real mother.'"

Despite the "grueling process" and concerns that she was "tempting God," or endangering her own or her baby's health by taking fertility drugs, Diane says she would do it again. "It was a journey of learning to count your blessings and deal with disappointment," she says. "During the process I had a miscarriage, mood swings, and a terrible allergic reaction to a progesterone shot. I wanted someone to tell me it was over—that it was time to move on. But it's really a miracle. A baby is such a joy and a gift."

## Fertility Forecasting

Yet what if scientists could help infertile women, especially older women, avoid the issue of donor eggs in the first place? "We're trying to understand what makes the best quality egg, because the more we know, the more we may be able to treat the eggs of older women, to make them act like young eggs," Powers says. "If a woman goes through IVF and we get 15 eggs, are some more likely than others to make an embryo? We'd like to know more about egg physiology and function so we can improve culture conditions."

"In New England," he adds, "we don't experiment on eggs or embryos that are going to be discarded; we take pictures of a living embryo with a microscope and quantify the images with computers to learn about the embryo's function without harming it." Powers adds that patients decide what to do with their unused embryos.

Another option on the horizon, notes Schultz, is freezing ovarian tissue or eggs. "The technology has been created, but has not been consistently success-

ful," she says. "Women who are worried about their future fertility could freeze their eggs or part of an ovary. But it is unclear what the ramifications are for the children and the safety of the pregnancy when women conceive after normal childbearing years. This is truly experimental in many ways."

Still another—though controversial and experimental—treatment to help older women involves transferring genetic material from one of their own eggs to the egg of a younger woman, after the DNA has been removed from the target egg. But the technique, sometimes called "nuclear transfer," "belongs in the experimental lab, with animal models," Powers says. "It's unethical to suggest otherwise. This is a treatment for an older woman with older eggs, but we don't know what the problem is with older eggs."

Ryan explains: "The question is, is it the cytoplasm or the nucleus that's at fault? It seems to me that both are in question."

## Treating Male Infertility

Infertility doesn't just affect women. Men account for 40 percent of infertility among couples, and the technology available to help them, too, has expanded in the last decade, bringing with it new questions.

A variety of sperm problems can account for male infertility. Sperm may be completely absent in the ejaculate, present in low concentrations, have poor motility, or have an increased percentage of abnormal shapes and forms. The procedure most commonly used to overcome male infertility problems is intracytoplasmic sperm injection (ICSI), which allows an embryologist to inject a single sperm directly into the cytoplasm of a mature egg using a microinjector pipette. ICSI can facilitate fertilization with sperm that will not bind to or penetrate an egg, and it

\*Names with an asterisk have been changed.





can be used in men with extremely low numbers of sperm.

"ICSI was a major breakthrough about seven years ago," Powers says. "If you just put one moving sperm and one egg in a dish, the odds are low of them coming together. Normally we mix 100,000 sperm for each egg, so ICSI helps us treat the case of a man who doesn't have 100,000 moving sperm."

Other procedures may need to be used in conjunction with ICSI, such as microsurgical epididymal sperm aspiration (MESA). First performed in 1985, MESA is a microsurgical procedure carried out in patients whose sperm cannot be obtained through ejaculation, explains Robert Oates, a urologist at Harvard Vanguard Medical Associates and Boston Medical Center. "These patients include those with congenital, unreconstructable blockages of their ductal system, or deficiencies in their sperm transport system," he says. "The basic concept is to extract sperm from portions of the epididymis that will

then be used in conjunction with advanced reproductive techniques in an attempt to achieve pregnancy."

But for men with non obstructive azoospermia, Oates points out, "sperm production is so poor that no sperm can be found in the ejaculate." For approximately half of these men, individual spermatozoa may be found in the testicular tissue itself, a harvesting procedure known as testicular sperm extraction (TESE). TESE is then used in conjunction with ICSI to achieve pregnancy.

#### **But What's Being Passed On?**

"Our technology has surpassed our understanding of what causes these sperm-deficiency conditions," Oates says. He points out that many genetically based syndromes result in reproductive dysfunction in men, and notes that when TESE and ICSI are used to achieve pregnancy, the result can be males with the same genetic abnormality.

Kallmann's syndrome, a condition of azoospermia occasionally due to a defect in a gene on the X chromosome that also affects olfactory nerves, is one example. "If we help a man with Kallmann's syndrome achieve a pregnancy with his wife, some of the consequences may be seen in his grandsons," Oates says. "We explain that his grandson through his daughter may be affected, and then it's a personal decision."

Infertility is a condition, he adds, "but there are many other diseases that people knowingly pass on, like Huntington's disease or sickle cell anemia or albinism, so we should not have a legislative mandate that this person cannot reproduce. Talk about a slippery slope. What about the man who's 4'2" or has bad eyesight?"

"How are we supposed to define the perfect human?" Oates adds, noting that as preimplantation genetics enables individuals to screen for more characteristics, as opposed to devastating diseases, there's potential for abuse.



# For everyone involved in the business of making babies, both the challenges and the rewards are plentiful.

"Think of depressive illness, which many talented artists have had. What a shame if we didn't transfer an embryo destined to be Hemingway because we knew it had manic-depressive disorder.

"What makes treating infertility different from treating other diseases is that it affects the next generations," he says, noting that "it's crucial to counsel patients on what is known and unknown about their situation before they decide to proceed with ICSI." He adds that tests are being developed to test sperm, rather than blood, for genetic mutations.

In the meantime, Oates says that his position should be "to do as much as I can for the patients. Only they can understand what this means for them." He does draw a line, however, at some procedures. "I don't agree with cloning at all," he says. "A cloned child wouldn't have his or her own genetic identity."

Ryan agrees, saying, "A child ought to be sought for his or her own sake."

Oates also balks at retrieving sperm posthumously, noting that he received a call last winter from a woman with that request. "I explained that I wouldn't perform the procedure because I didn't know whether that had been the man's desire," he says. "You can't take his organs without consent—I don't think you should be able to take his tissues either. What if it were a woman in a coma? Would we give her medication to make eggs and then harvest them?"

## Turning to Sperm Donors

Even artificial insemination, a reproductive option that has long been used to help heterosexual couples, has led to a different set of concerns for both patients and clinicians in recent years.

Kelly\* and Judy,\* a lesbian couple in their thirties, decided to use a sperm bank because they knew that adoption would not be an easy route for them. Kelly eventually got pregnant using anonymous donor sperm and intrauter-

ine insemination and gave birth to a healthy boy. Still, she felt guilty about having a son with no father in the picture. "We know men who will act as role models," she says, "but I worried about depriving him of the chance to see his own identity reflected in his father."

At first, Kelly says, they spent hours poring over sperm donors' essays. "We first screened for medical problems," she says. "Then we tried to screen for character and motive. If he saw a sister suffer through fertility problems, that was more appealing than someone who just wanted a new stereo. But then we got more cavalier—anyone tall with light colored eyes was great. Not that we would be fooling anybody, but we wanted to combine our physical traits."

Kelly points out that the process was far from easy. "Arduous is a fair description," she says. "It was extraordinarily stressful and expensive. But when we look at our son, all our worries dissolve. He's so beautiful and so well loved."

Ungerleider Springer met with another lesbian couple whose request was more complicated. "Neither woman had a history of infertility," she says. "They both wanted to get pregnant, but instead of just using donor sperm, each wanted to go through an IVF cycle, fertilize her eggs with donor sperm, and transfer the embryo to the other woman. Should you do that for psychological reasons when there's no medical indication?" After her team members discussed the risk factors—including a slightly higher incidence of premature delivery with IVF—and after they considered the appropriate use of resources, they decided not to grant the couple's request.

Whether it is the clinician or the patient who must make the decision to end infertility treatment, Steinberg says, mental health specialists can be helpful. "Patients need to grieve the fact that they may not have a genetically related child," she explains. "We need

to help them understand that they've given the technology a fair chance."

## The Core Questions

Although people undergoing infertility treatment and any resulting offspring are most affected by the issues raised by ART, society's values become part of the broader ethical discussion.

Most infertility programs work with an advisory board charged with reviewing the procedures that might raise ethical questions. At Brigham and Women's Hospital, Barbieri says, "the doctors' mandate is to care for patients, but also to be aware that society is monitoring our medical practice. I view our ethics committee—which includes three clinicians, an ethicist, a judge, a law school professor, a hospital attorney, a chaplain, and a social worker—as collectively representing the diverse views of society."

Ryan points out that the core of ethical problems for reproductive biology "goes back to the tension about abortion and the rights of women versus the interests of society. After that, the largest issues associated with reproductive technology are typified by IVF, and the recurring argument from the Catholic Church that any assisted reproduction is illicit. Having said that, the questions are whether it's safe, then what impact it will have on the child, and then what impact it will have on the family and society."

For everyone involved in the business of making babies, both the challenges and the rewards are plentiful.

"You get a great reverence for human life when you work with embryos in the laboratory," Powers says. "It's an honor and a responsibility to hold a human embryo in a pipette, especially when that embryo walks in the door as a two-year-old child to say hello." ■

*Phyllis L. Fagell is associate editor of the Harvard Medical Alumni Bulletin.*

# The Doctor's DILEMMA

Ethical quandaries can leave the best-trained physicians struggling for answers

"IF HIS WIFE THOUGHT HE WAS BETTER OFF dead, why did she call 911?"

One member of the hospital's ethics committee tried to explain the situation to another: "She hadn't planned to call for help, but the blood oozing from the knife wound in his neck was too unsettling. She panicked. When the ambulance arrived, she knew she'd made a mistake."

"Was she the appropriate surrogate decision-maker?"

"Absolutely. He was obtunded, and she was both his next of kin and his legally designated health care agent. In fact, as she blocked the gurney, she waved his proxy document so there would be no doubt as to who was calling the shots."

"She blocked the gurney?"

"Yes—he was all ready to go into the operating room when she said, 'You're not taking him to surgery.'"

"What did the surgeon do?"

"He was very upset. He had a patient with a hole in his left carotid artery who

needed immediate surgery, and the man's wife, who had the legal power to make decisions, was yelling, 'If you touch my husband, I'll have you arrested for assault and battery!'"

"Either the woman was crazy, or evil, or there's more to the story."

There often is more to such stories. In this case—which happened several years ago and led the surgeon to seek help from the hospital's ethics committee—the man's children told the social worker that their parents had been devoted to each other for 42 years. Their mother's obstructionism was, in fact, rooted in a deep concern for her husband's welfare.

For 15 years, the man had suffered from severe depression. He had tried antidepressants and electroshock therapy, yet nothing had worked. He told his family he didn't want to continue living in what was, for him, a state worse than death. When he plunged the knife into his neck, his wife and children, who had

*by* DAVID STEINBERG



WIA



# I was deeply conflicted, because I wanted to respect my patient's should die from an unanticipated, easily correctable problem

watched his prolonged agony, hoped he would find peace at last.

The emergency room doctors questioned whether a morbidly depressed man was capable of meaningful decision-making. They knew that, in emergencies, it's often best to take all possible measures to preserve life. Death is a choice that cannot be reversed.

In this case, the dilemma was resolved before the ethics committee could respond. In the midst of the emergency room tumult, the flimsy clot that had sealed the hole in the man's carotid artery lifted off. The fatal hemorrhagic gush that ensued was indifferent to the surgeon's unresolved ethical dilemma.

Ethics has become an inescapable and vital part of clinical practice. During my early years as a hematologist, I focused on learning medicine. Yet many of the decisions I had to make—how much to tell patients when their prognosis was dismal, when to withdraw life supports—were not simply technical, medical judgments; they also often required the negotiation of conflicting values.

Ethical dilemmas have become so integral to the practice of medicine, in fact, that the Joint Commission on Accreditation of Health Care Organizations now requires health care facilities seeking its imprimatur to have a mechanism for dealing with ethical conflict. As a result, many hospitals have ethics consultants or committees.

## And Baby Makes Six

Many ethical concerns arise because technical advances become available before we can fully understand their implications. The ability to culture human embryonic stem cells, for example, holds great promise, yet has created controversy about the moral status of those cells. And assisted reproductive technologies, which, when called on for a dramatic performance, can gather five people together for the enterprise of making a baby, have

turned a seemingly simple question—who should be considered a baby's parents—into a matter of contention.

In California, Luanne and John Buzzanca used donated sperm, a donated egg, and a gestational surrogate mother to make a baby. Before the baby was born, the couple separated and John Buzzanca, to avoid paying child support, argued that he should not be considered the father. The court decided that although Buzzanca was not the genetic father, he was instrumental in arranging the baby's conception and birth, and ordered that he pay child support.

## Colliding Principles

Sometimes two valid principles collide under circumstances that make it impossible to honor one without violating the other. The clash between respect for patient autonomy and the principle of beneficence, for example, has caused me significant angst over the years. A troubling incident involving a patient I'll call George Warner illustrates this conundrum.

Warner, a 74 year old retired plumber, had slowly progressive, incurable cancer. In the context of a discussion about his disease, he had mentioned that he would not want to be placed on a respirator. Despite his cancer, he felt reasonably well until he was admitted to the hospital with pneumonia. A few hours later, he suddenly became extremely short of breath, and his blood pressure fell precipitously. A chest x-ray revealed a collapsed right lung, probably caused by a mucous plug. We could easily resolve the problem by suctioning the mucous through a bronchoscope. To do this safely, however, would require Warner to be on a respirator for several days.

I was deeply conflicted, because I wanted to respect my patient's wish not to be placed on a respirator, but I didn't think he should die from an unanticipated, easily correctable problem when he had minimal cancer and a good quality

of life. I could not respect my patient's choice and, at the same time, act in what I believed to be his best interest.

I discussed my anguish with Warner's wife, who agreed to the bronchoscopy and the respirator. I suffered a few sleepless nights; fortunately, when Warner recovered from this episode, he told me that he agreed with my decision. But this story could easily have had an unhappy ending, filled with recrimination and guilt.

## Shades of Gray

Other clinical dilemmas stem from inherent conflicts, such as the one between a pregnant woman and her fetus. Innovative surgery that may benefit the fetus, for example, compels us to define an acceptable level of risk to the mother. And, in a controversial decision, a South Carolina court, forced to balance fetal and maternal rights, used the state's child abuse laws to sentence a woman to eight years in prison because she had placed her fetus at risk by using cocaine while pregnant.

The probabilistic nature of medicine also generates ethical conflicts over the withholding and withdrawing of therapy. These are not merely theoretical questions for me, because I work with very sick patients. When they are in crisis, it is often impossible to predict whether their future holds recovery and a period of good living, or a fruitless struggle and inevitable death.

I would not treat a patient if I knew the chance of success was zero; the converse would hold true if the chance of success was 100 percent. In the clinical arena, the odds often lie between those numbers and are tinged with uncertainty. Does a 20 percent likelihood of success warrant vigorous therapeutic intervention? What about 8 percent? Where do we draw the line, and why? These questions have no generally accepted answers, and physicians and families are often left to agonize over therapeutic decisions that present as ethical dilemmas.



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Another area of conflict lies in the paucity of resources, which forces us to consider how to fairly dispense scarce organs, intensive care unit beds, and other limited health care resources. Congress has debated how best to distribute donor hearts and livers to patients at risk of dying while languishing on a waiting list.

The lack of consensus on such basic issues as when life begins and ends creates another wellspring of ethical conflict. The abortion debate, for example, continues without resolution. And some institutions have modified the definition of death and harvested organs after a patient's heart has stopped beating for two minutes because, at that point, recovery is highly improbable and organs are still salvageable. Critics argue, however, that this approach violates the "dead donor rule," because at two minutes the whole brain, and therefore the patient, may not be dead.

### A Multidisciplinary Approach

Bioethical dilemmas generate cries for help, because they are urgent and resistant to resolution. Although many people still turn to religion for answers, in recent decades, there has been a moral shift toward the philosophic tradition of secular ethics. Priests, ministers, and rabbis have been joined by a relatively new professional, the bioethicist. The voices of these bioethicists are heard in the media, in scholarly and public policy forums, and in the more intimate world of clinical medicine.

The best descriptive term for bioethicists is "multidisciplinary." An expertise in medical ethics requires neither a specific academic degree nor formal credentialing. Physicians, nurses, theologians, lawyers, social workers, philosophers, sociologists, and other thoughtful professionals have all entered the arena. Their legitimacy rests on the multidimensional nature of ethical problems, which demands analysis from a variety of

perspectives. Lawyers contribute the legal perspective, theologians the doctrinal and spiritual, social workers the cross-cultural, and philosophers the analytical and theoretical. My primary contribution would be a perspective rooted in years of clinical experience.

In the hectic world of medicine, ethicists provide clinicians with the opportunity to discuss problems and to share the stresses that come with caring for the sick. Ethicists' more formal contributions can be divided into three components: empirical, analytical, and moral.

In their empirical mode, ethicists provide relevant facts. What is the hospital's policy on removing respirators? What is the risk to people who want to donate a lobe of their liver? How accurate is genetic testing for breast cancer? Ethical dilemmas are unlikely to find a sound resolution without a full understanding of the relevant facts; we are indebted to ethicists when they make that information available.

Many ethical dilemmas are more complex than they first appear. Careful analysis can reveal the intricate dimensions of a problem and define the principles and values at stake. In analyzing whether a request to retrieve sperm from a dead man for posthumous procreation should be granted, for example, an ethicist might weigh the rights of the dead, the demands of informed consent, the meaning of genetic identity, the interests of the unborn child, the emotional and property interests of the deceased's family, and any relevant laws. Ethical analysis may be the most important contribution of bioethicists, whose expertise has been said to rest not on the positions they adopt, but on their ability to provide a justification for those positions.

Bioethics becomes most problematic in its moral mode, in which relative values are weighed to reach the answer we want—what's right and what's wrong. An ethicist's conclusions are ultimately contingent on the moral theory from which they are derived. Unfortunately,

there is no consensus on a uniform moral theory.

Some ethicists, for example, are utilitarians who define the right course of action as being the one that brings the most good to the most people. In Oregon, a list of medical procedures is ranked in order of their perceived benefits. Depending on the available budget, a line is drawn and Medicaid patients are not covered for conditions below that line. This approach is justified on utilitarian grounds, because it brings the most good to the most people.

Other ethicists find moral bedrock in Aristotelian virtues such as trustfulness, prudence, and fortitude. One popular approach to ethics is rooted in respect for four nearly inviolable principles: respect for personal autonomy (inform and permit the patient to make unmanipulated decisions); non maleficence (do no harm); beneficence (do good); and justice (distribute limited resources fairly).

Many of these and other secular approaches to morality can be combined to varying degrees. Add cultural and religious coloration, and variety in the ethical repertoire expands further. Bioethicists with respectable credentials can be found taking opposing positions on most moral issues, suggesting that bioethicists cannot distinguish right from wrong any better than the rest of us.

What does this mean when we encounter ethicists in clinical settings? We can learn from their empirical and analytical contributions, and we should listen to their moral conclusions. When ethical issues arise, though, we must recognize their conflicting methods and conclusions—and their fallibility. Ultimately, each of us must seek the answers to troubling questions in the depths of our own moral consciousness. ■

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# Slicing the PIE

When limited health care resources  
must be divided, patients often reveal  
their sense of fairness

**I**N 1995, JUST DAYS AFTER I HAD ARRIVED IN LONDON FOR A three-month sabbatical to study the ethics of resource allocation in the National Health Service, the issues I was investigating hit the front page. The morning newspaper headline read, "Leukemia Girl Loses Court Fight."

Five years earlier, Jaymee Bowen, known at the time as "Child B," had developed non-Hodgkin's lymphoma at age six. In December 1993, Jaymee was found to have acute myeloid leukemia, for which she received a bone marrow transplant in March 1994. The leukemia recurred the following January.

On clinical grounds, Jaymee's doctors recommended against more chemotherapy and a second bone marrow transplant, believing that the likelihood of response was extremely small. Jaymee's father, however, found specialists who were more optimistic about the potential of further treatment, and he appealed to the Cambridge Health Authority—the British equivalent of the insurer—to cover the treatment. When the Health Authority refused to pay for the £75,000 regimen, citing the need to set priorities within its limited resources, Jaymee's father sued.

by JAMES E. SABIN





# By recognizing about our patients what we know about simply atoms of individual need and desire—we can

Jaymee's heartwrenching situation provides an opportunity to contrast the ways in which the United Kingdom and the United States handle tragic choice situations. With the exception of the process leading up to the Oregon Health Plan in 1989, there has been little in-depth public dialogue about the ethics of resource allocation in the United States. Our main forums have been cinema, television, and sensationalistic journalism. Movies such as *The Rainmaker* and *As Good as It Gets* portray the ethical issues as a Manichean struggle between needy patients and criminal insurers. Although medical journals have published cost-effectiveness analyses that illuminate the complexities of the situation, these articles are read more attentively by policy wonks than by political leaders or the public.

In contrast, the court process in London was impressively forthright. The first level judge ordered the Cambridge Health Authority to reconsider, saying that "where the question is whether the life of a ten-year-old girl might be saved, by however slim a chance, the responsible authority must in my judgment do more than toll the bell of tight resources."

The Court of Appeals, however, reversed the lower court, writing that "in a perfect world any treatment which a patient, or a patient's family, sought would be provided if doctors were willing to give it, no matter how much it cost, particularly when a life was potentially at stake. It would, however, be shutting one's eyes to the real world if the court were to proceed on the basis that we do live in such a world. Difficult and agonizing decisions have to be made as to how a limited budget is best allocated to the maximum advantage of the maximum number of patients."

Jaymee's dilemma disappeared from public view two days after the headline appeared, when an anonymous donor provided £75,000 to pay for chemotherapy and a donor lymphocyte infusion.

The treatment provided a brief remission, but the leukemia recurred and Jaymee died in May 1996. Since her death, however, the issues her treatment raised have received thoughtful attention in the United Kingdom.

BECAUSE THE UNITED STATES spends more than twice as much per capita on health care than the United Kingdom, we rarely encounter resource allocation issues in as raw a form as Jaymee and the Cambridge Health Authority did. Despite our wealth, however, the expansion of promising new treatments, combined with aging populations, makes living within a budget a difficult but unavoidable challenge. Good preventive medicine, broader use of well-conceived guidelines, and aggressive improvement of health care quality will allow us to get more mileage from our health care expenditures. But the tension between individual desires and community resources is a fact of social existence.

Unfortunately, for at least 20 years our health care strategy has tried to avoid this inescapable tension. We have asked the market to allocate resources without acknowledging that limits must be set. As a result, we have not been able to engage in meaningful political deliberation about how to allocate resources in the most ethical manner. Until we find a constructive way to discuss how to do our best within reasonable limits, public distrust of the health care system will continue to escalate. We physicians and medical educators can play a crucial role in helping society make hard choices in a responsible, compassionate manner. Although we cannot fully compensate for the lack of political leadership on these issues, we can make a difference, much as we have done with end-of-life care.

When I attended HMS, I was taught that revealing the truth about terminal illness was cruel, destroyed hope, and showed poor medical judgment. Medical students today are taught the opposite—that trying to help patients understand and deal with the painful realities of terminal illness is sound practice. We are doing a better job of helping students talk with patients and families in an empathic, trust-building manner, and we are doing so in our own practices. If we have learned to help ourselves, our patients, and the public deal better with mortality—the ultimate form of limit—we must be capable of doing the same in creating guidelines for health care expenditures. But how can we do this?

Our patients will probably be our best teachers. Conversations with patients and families that are ultimately about resource allocation issues have been among my most humanly rich and surprising encounters. These exchanges have convinced me that the dominant ethical paradigm we assert for our profession inaccurately portrays our patients as islands of pure narcissism and pays too little attention to human interconnectedness.

The biggest impediment to helping our patients deal with resource limits is the belief that ethical physicians should think only about the welfare of individual patients. We believe that in our clinical role we should consider benefits and harms to individual patients and not costs to society. If we do otherwise, we will become unethical double agents, and our patients will not—and should not—trust us. Experience leads me to question this view.

Six years ago my mental health colleagues in what was then called Harvard Community Health Plan concluded—with the help of our members—that we needed to offer more outpatient care to our sickest patients. Although we were not given additional money, we were



ourselves—that we are attached to others and not inch toward a broadened medical ethic.

allowed to set new priorities. We concluded that we could increase services to the sickest patients only by requiring a new payment from the less sick after their eighth outpatient appointment.

After we made this change, my colleagues and I talked with our patients about the new policy. With patients who were eligible for more services, such as those with schizophrenia, we said, “The bad news, as you know, is that you suffer from a severe illness. The good

rupt an appointment with one patient to attend to an emergency with another.

No one was happy about paying the new fee. But no one thought the policy was unfair. Our patients understood that we could not cover every beneficial service. Giving priority to the sicker members seemed sensible and fair.

Of course patients can trust us only if they believe that we are passionately committed to their welfare. But I have been impressed with how often my

ended medical ethic. The assertion that patients will trust us only if we focus solely on what benefits them as individuals is a hypothesis, not a proven fact. It overlooks the degree to which our patients and the public at large harbor concerns for others.

Toward the end of his life, my father, twice a widower, married again. Shortly after the wedding, my new stepmother, whom he had known for only a few months, began to show signs of dementia. My father had macular degeneration, and caring for a spouse with dementia was extremely difficult. I was concerned about him, and I gently asked if he felt he had to take care of someone he had not known long. His answer was reproachful but instructive: “How many ways can a blind 87-year-old be useful in this world? Of course I will take care of her!”

For more than 70 years, Francis Weld Peabody’s eloquent lecture on “The Care of the Patient” has provided HMS graduates with an ethical compass. I doubt that I am alone in feeling that I could quote the final 14 words of Peabody’s beautiful talk—“the secret of the care of the patient is in caring for the patient”—more easily than I could answer board questions in my specialty.

But the key ethical guidance for the next decade is actually buried in the first 12 words of that famous sentence—“One of the essential qualities of the clinician is interest in humanity.” We need to help patients, families, and the public develop an ethic that cares about both the individual and the wider community. That caring is what ethical resource allocation is all about. Properly understood, Peabody teaches us that ethical physicians must embrace responsibility for the common good as well as the welfare of individual patients. ■

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news is that we now have more outpatient treatment resources available.” With our healthier patients, we had the opposite conversation: “The good news is that even though you have some significant problems, you do not have a severe illness. The bad news is that after eight sessions there is now a new fee.”

We did not present cost-effectiveness analyses or complex ethical arguments about resource allocation. We used simple, commonsense terms that made fundamental human sense. To most members, the policy had the same kind of obvious logic as when we inter-

patients ask me to consider the welfare of others—usually the welfare of family members and friends, but often that of the wider community. They say things like: “I don’t want to take away from what my children have in the future”; “I want to take part in a study so I can contribute to others”; and “I am sure there are other patients whose need is greater than mine.”

By recognizing about our patients what we know about ourselves—that we are attached to others and not simply atoms of individual need and desire—we can inch toward a broad-

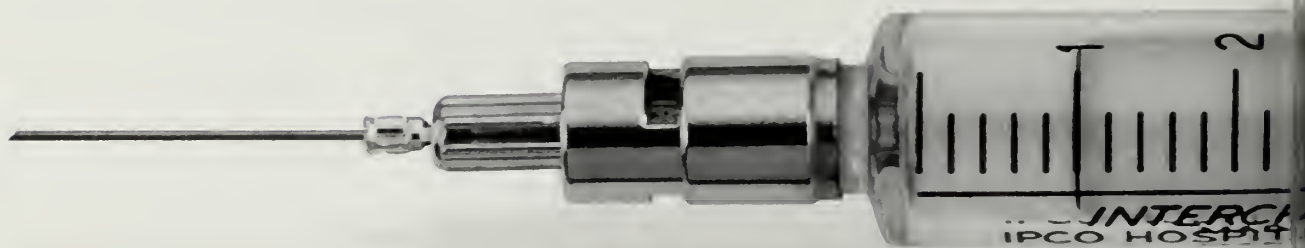
# Beyond

JACK KE  
Now that the doctor most associated with physician-assisted suicide is in prison

JUST OVER A YEAR AGO, JACK KEVORKIAN stared down millions from the television screen. Viewers watched him smile and banter with Mike Wallace, then, in a videotaped replay, administer a lethal injection to Thomas Youk, a Detroit man suffering from amyotrophic lateral sclerosis. Five months later, the controversy triggered by the televised spectacle of Youk's death sparked yet more national discussion

when Kevorkian was sent to prison on murder charges.

Whether one agrees or disagrees with Kevorkian's actions, the highly charged debate has helped us reflect on the values, hopes, and anxieties that we as physicians and as patients share about dying. We wish, in the final days of our lives, to be free of suffering, to maintain control, and to surround ourselves with a commu-





# KEVORKIAN

can the debate continue in a more reasoned way? • *by* JOSHUA HAUSER

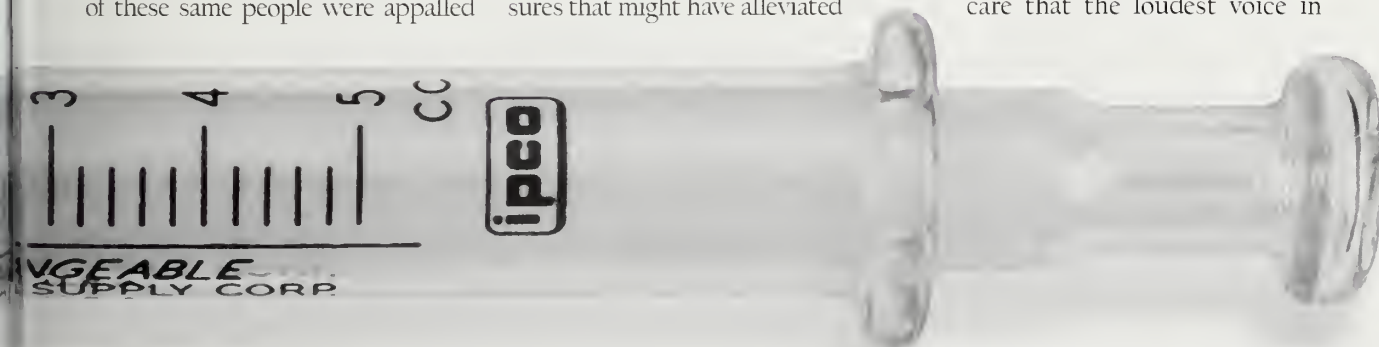
nity of family and friends. With Kevorkian's conviction, we can shift the focus from critiquing his actions to ensuring that we help our dying patients and their families achieve those desires.

Many physicians, nurses, chaplains, social workers, and, most of all, patients and families, have thought deeply about end-of-life issues. Many of these same people were appalled

by what they perceived to be the indignities in Kevorkian's string of more than 100 physician-assisted suicides and, in particular, in Thomas Youk's videotaped death. Members of both the medical community and the media have raised troubling questions about Youk's death, from Kevorkian's cursory nod to obtaining "consent," to his disregard of measures that might have alleviated

Youk's symptoms (such as medications to decrease secretions and relieve the sensation of choking), to the absence of family members or any other health care professionals.

In the view of many health care professionals, including myself, it is indeed both sad and counterproductive to the establishment of sound guidelines for end-of-life care that the loudest voice in



# In the end, Kevorkian's story has emphasized that end-of-life care More broadly, it is about the life experiences of patients and their

this debate has been the cold tone of Jack Kevorkian. We would argue that our emphasis should be on care and comfort, not on efficiency and ease. As physicians, we must focus not on the death itself, but on maintaining quality of life during the hours, days, and months before someone dies.

A discussion of three integral values—alleviating suffering, preserving autonomy, and maintaining community—represents a more appropriate starting point than debates about the morality and legality of physician-assisted suicide. Realigning our focus on these values shifts our attention away from Kevorkian and more properly toward patients and their families. We need to reframe the debate by asking one basic question: What do patients and their families need and want in end-of-life situations?

First, what do we mean by suffering? Physical, psychological, spiritual, and existential suffering take myriad forms, and we must strive to understand and alleviate them all. The experience of suffering varies widely among patients and their families, and relieving it is more central to the role of physicians than either fighting or embracing death. To begin to understand each individual's experience requires more than medicine and much more than a lethal injection; it takes time, patience, and caring.

Second, we must think deeply about the notion of autonomy. How do we maintain control over our lives, and when do we cede this control? Patient autonomy, which is a crucial value throughout medicine, does not exist in a vacuum. The influence of family members, physicians, and others on patients' choices is profound and must be recognized and explored. Physician-assisted suicide raises many questions about how patients, families, and doctors communicate and act in end-of-life situations. Clearly, part of the desire for physician-assisted suicide is the wish to

preserve control, but the meaning of such control can be complex, and it therefore requires a more thoughtful and sophisticated examination than that which can be provided in a "60 Minutes" segment. Were there other ways, for example, besides allowing Kevorkian to give him a lethal injection, that Youk could have preserved some control over his life and his body?

Then we must think about community. How do we come together as patients, doctors, families, and members of various communities to care for each other and consider these issues? Some patients may want to die alone, while others may want to be with loved ones. Physicians should strive to understand these preferences. We know, on the basis of the televised videotape, that Youk died alone, a circumstance that raises questions about whether he wanted it that way. End-of-life care should take place in an environment open enough to allow patients and their families to express and realize such choices. Physician-assisted suicide, as practiced by Kevorkian, makes this impossible.

Although Kevorkian's conviction has brought some closure to one part of this debate, these issues will not—and should not—disappear. The disagreement between the Michigan judge who sentenced Kevorkian and Youk's wife and brother adds a new wrinkle to this discussion. Their words revealed the potentially conflicting roles of the law and families in end-of-life care, suggesting that the gulf between the law and families, whether perceived or real, is wide.

In addressing Kevorkian, Judge Jessica Cooper wrote, "This trial was not about the political or moral correctness of euthanasia. It was about you, sir. It was about lawlessness." Yet Youk's widow was quoted as saying that her husband "would be greatly distressed that the man who brought him peace at the end would now suffer on his

account." And Youk's brother added, "History will judge us harshly for such a lack of insight and compassion."

Clearly, individual interpretations of the "moral correctness" of Kevorkian's actions and individual views of compassion are central to the ongoing debate among physicians, patients, and families.



Mike Wallace (left) and Jack Kevorkian



is not—and must not be—only about physician-assisted suicide. families. And it is about suffering, autonomy, and community.



in the lobby of a Michigan hotel where Wallace interviewed the euthanasia advocate for the controversial "60 Minutes" broadcast.

But the law cannot address all the decisions patients and their families must make. Discussions among patients, their families, and their caregivers will allow us to pursue a richer understanding of serious illness and compassionate end-of-life care.

In the end, Kevorkian's story has emphasized that end-of-life care is not—

and must not be—only about physician-assisted suicide. More broadly, it is about the life experiences of patients and their families. And it is about suffering, autonomy, and community. As physicians, we can hope that, in the new century, we will conduct a responsible discussion, away from the glow of television and the

spectacle of Jack Kevorkian. These issues are too important to be ignored, and too profound to be debated according to an agenda set by any one individual. ■

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Do patients have the right to decide when their time is up?

# WHOSE DEATH is it, anyway?

"WHY DO YOU WANT TO DO THIS?" I ASKED. As a doctor being asked to prescribe a terminal dose of medication, I thought my question seemed fair. I had, after all, an absolute responsibility to determine mental competence, a motivation free from outside pressure, and the lack of an overriding, possibly temporary or treatable psychiatric illness.

Jim,\* sitting across from me, was composed, intent, and dead serious. In his forties, he had labored after his brain biopsy to adjust to the diagnosis of a high-grade astrocytoma, a brain

tumor whose typical prognosis is measured in months. After a round of consultations and second opinions and a review of the good, the bad, and the ridiculous on the Internet, he knew that a temporary remission after radiation therapy was possible. But, lacking divine intervention, his prognosis was still poor.

"I don't want to live without control of my body," he said. "I've been told that I'll have no pain, but I'll lose control of my body and mind, bit by bit, and I don't want to live like that."

*by* PETER M. PATRICELLI





I sat in front of her and extended my hand, which she took with nooooooo...nooooooo...nooooooo!" She put my hand to her cheek

I assured him that if he didn't choose to end his life, we could take measures to ensure that when he lost consciousness, he would linger only a few days more, without pain or awareness.

He shook his head emphatically.

"I don't want even a few days of a vegetable existence. And I don't want to see myself disintegrate."

As Jim spoke, his mother sat beside him, dabbing at moist eyes, but solid and supportive. "I don't want Jim to die, or leave one day sooner than necessary," she said. "I want him with me under any circumstances as long as possible. But if this is what he wants, then all I can do now is support him and see that his will is done."

After I finished my evaluation, I explained to Jim that he still had much to go through. "I hope the radiation therapy will help, but there are many uncertainties," I said. "I think we should go through the whole process now, get all our ducks in order. The critical issue will be timing. You wouldn't want to do anything too quickly, while you still have meaningful life to live. The danger, though, would be in waiting too long and risking a sudden brain event that might cause you to lose the ability to carry this out."

Flanked by his parents, Jim walked out with the ironic plan of pursuing the gritty details of both life-seeking and death-enabling treatments. Both would be near disasters.

### Where Is Thy Sting?

**I**n Oregon, where I practice family medicine, the Death with Dignity Act allows terminally ill Oregon residents to obtain prescriptions for self-administered, lethal medications. This act, which was implemented in 1997, states that ending one's life in accordance with the law does not constitute suicide. Yet the

U.S. Congress is debating the "Pain Relief Promotion Act of 1999," which could affect Oregon's law, as it would make it illegal to use scheduled drugs to hasten a death. Anyone "intentionally dispensing, distributing, or administering a controlled substance for the purpose of causing death or assisting another person in causing death" could be prosecuted and given a prison term of 20 years to life.

For me, the galvanizing experience in thinking about terminal patients' rights came not long after I finished my medical training. A patient,

Mabel, sat in front of me for the first time 25 years ago as an independent, intelligent, professional woman who knew what she wanted and was used to getting it. She had her end-of-life decision-making written out, signed, and even notarized. The first thing she said after greeting me was, "I want you to be aware of my strong wish that, should I ever reach a point in my life that I am confined to a nursing home, or lose my ability to care for myself or interact meaningfully with other people, I don't want my life prolonged under any circumstances."



PHOTO: NITA ZWISLER



her left and held between us as she pleaded, “Nooooooo... and again cried, “Nooooooo...noooooooo...noooooooo!”

I listened carefully and told her that I understood and, within the limits of the law, would do my best to comply with her wishes.

“I don’t owe anything of my life to anyone,” she told me. “I have always been on my own, and my work has been my life. Now I’m retired. When I can no longer live my life to my satisfaction, then I don’t want to exist any longer.”

It was easy to nod in agreement, with her sitting whole and healthy in front of me. Two months later, during a medical procedure to head off a

threatened stroke, the stroke won, robbing her of speech and motor control of her right arm and leg. Without today’s sophisticated diagnostic tools, it was impossible to predict how much recovery was possible, and it was then considered legally risky to withhold intravenous fluids. She had to be revived enough for us to discover how devastated her brain had been. Then she was sent to a nursing home, where her brain recovered from the fog of acute injury only for her to discover, to her horror, that her worst possible nightmare had come true.

A month later, on my first visit to the nursing home, she was sitting in a wheelchair in a large room filled with residents and staff. She saw me from a distance as I entered the room.

“Nooooooo!”

The scream stopped all noise and movement in the room. My eyes sought the source of the scream. I recognized the twisted face and took the full pierce of its meaning in a single second.

“Nooooooo!” Mabel repeated, bending forward at the waist and pushing vaguely and ineffectually on one wheel with her only working hand in an attempt to get to me. “Nooooooo!”

Attendants and nurses supported her as I approached. She had and would forever have only one word—“Nooooooo!”—with which she could stab, dismiss, or plead, depending on her level of anger.

I sat in front of her and extended my hand, which she took with her left and held between us as she pleaded, “Nooooooo...noooooooo...noooooooo...noooooooo!” She put my hand to her cheek and again cried, “Nooooooo...noooooooo...noooooooo!” The nurses told me she had not meaningfully spoken until then. I left the nursing home sucked dry of all emotion.

A month later, with fear and trepidation, I visited again, and the scene was repeated. In the ensuing months, the staff asked that I call before my visits so that they could isolate her from the other residents and, I suspect, prepare themselves for her outbursts.

Over the next six years, Mabel took antidepressants and still pleaded her unmistakable case. She tried starving herself, but when she became too weak to resist, the staff would feed her. When she developed seizures, she tried refusing medication, only to bring on even stronger seizures, which required hospitalization and treatment. She tried, over and over, to end



Jim stares for a moment, then begins nodding. "Sleep," he manages. He cants them, lays his cheek on his hands in the universal sign of

her life. And I tried, over and over, pushing hard within the limits of the law, to let her life end. To no avail.

Eventually I had to withdraw as her physician. I couldn't take the gut-ripping experience of her pleading any more, because I agreed with her utterly and yet was powerless. She lived eight more years. And I was left wondering what right societies and governments have to make demands on people in end-of-life situations.

### Shuffling Off This Mortal Coil

Jim's consultation to fulfill the requirements to get the end-of-life medication is a disaster. The specialist who had offered himself as the necessary second opinion tells Jim he can't possibly participate, because his practice and building are owned by Sacred Heart Hospital, and he hadn't realized he would have to sign anything. According to Jim's parents, the specialist then dismissed the three of them with few words and fewer minutes. They are furious.

Worse, I then receive a four-page "consultation" from the specialist in which he laboriously details a complete examination and states that Jim is *not* terminal, may survive 18 months or more, and, with a response to some newer experimental drugs, possibly considerably longer than that. The report is in direct conflict with this same doctor's clinical notes before any mention of end-of-life medication, and it counters the prognosis of other specialists. The optimistic prognosis also is based on treatments that Jim and his family have already rejected as too toxic and too unlikely to result in a remission.

My reluctant conclusion is that this doctor deliberately set out to sabotage the process. I call another

specialist to confirm the original prognosis and to analyze the illogical optimism in this letter.

I toss out the report, but the damage has been done. Time has been lost, and Jim's condition is worsening. The unnecessary pain and anger this episode has caused him and his family is incalculable. I must quickly find another doctor to serve as a consultant. The legal process before the medication can be dispensed is complex, precise, and—if not done right—possibly unforgiving. Jim is about to start the radiation therapy, his only hope for even a minor remission. It also could backfire and hasten his end.

Jim's radiation therapy does indeed backfire. The tumor swells in his skull, leaving little room for his brain. He is hospitalized, teetering on coma. Our hope is that, with treatment, his condition is only temporary and can be reversed.

We still do not have a signed consultation. My second choice of doctor is deemed risky, because his professional connection to me is too close. Jim's parents are panicked. Unless he recovers enough to allow a complete mental evaluation by a doctor new to the case, there seems to be no hope of getting the necessary second consultation.

Jim recovers enough to be discharged from the hospital to his parents' home and care, but then he begins to deteriorate again. In the first single stroke of good luck in six months, another specialist familiar with the case steps forward and says that he is willing to sign a form verifying Jim's prognosis and mental competency when he requested end-of-life medication several months back. Would that be sufficient? My contacts and legal consultations indicate that it will.

When the consultation form is received, only one step remains. I must determine that Jim is still men-

tally competent, that when he drinks the medication, he understands the consequences. Actually, the doctors who drafted the Oregon legislation had a difference of opinion on this point, but my own personal ethics and a bit of legal paranoia make me decide to ask Jim's parents to bring him to the office for a final evaluation. They say they will be there in an hour.

Helped in by his parents, Jim stares with a blank expression. Much has happened medically over the past two weeks, but the details are irrelevant. He has reached the point at which further treatment for any purpose other than to relieve pain or suffering is at best useless, unwarranted meddling that could serve just to prolong a situation that he has already declared to be unacceptable. The only question still on the table is whether he understands the consequences of taking the medication I can now legally prescribe to him, and whether he still wants to use it.

"Jim, do you remember who I am and the discussions we had about your taking medicine to end your life?"

Jim reacts with a visible internal struggle, and I don't know whether his block is in receiving and processing my question, or in articulating an answer, but clearly the question is too complicated.

"Jim, do you want the medicine to put you to sleep?"

Jim stares for a moment, then begins nodding. "Sleep," he manages. He puts his hands together as though starting a prayer, then cants them, lays his cheek on his hands in the universal sign of sleep, and nods vigorously, emphatically.

"I think that's clear," his father says.

The only remaining act is to get the medication to them as quickly as possible. I give final instructions, say goodbye to Jim and his parents, and then, alone, I cry.



He puts his hands together as though starting a prayer, then sleep, and nods vigorously, emphatically.



Minnie is someone I would not have wanted to cross when she was to herself about the cancer cells. "I'll get those suckers any way

### The Sleep of Death

When I pulled into the driveway, the house seemed unnaturally quiet and isolated, a house turned inward. Harold, thin and pale, was sitting at the dining room table next to his oxygen tank, with the oxygen line running to his nasal tube. In front of him was a pile of small medical devices. An engineer who had lived with an oxygen tank for 13 years, he had invented a simple clasp device to help control oxygen lines. He was assembling them to give to nursing homes and hospitals. The muscular work required for his thumb and forefinger to pick up the equivalent of a paper clip and snap it to a thin plastic necklace took all the oxygen his one remaining and damaged lung could supply and still allow his brain to function. He would assemble the necklaces for half an hour, then he would rest and maybe sleep. He felt the devices were his one contribution to society.

Nine months ago, Harold had been given six months to live. Respiratory failure is notoriously hard to predict, but for Harold, there was no question about the outcome. Each day he lost more weight, and his brain struggled to function with less oxygen and more retained carbon dioxide. And each day he continued to smoke, by maneuvering the cigarettes around his nasal tube.

The first physician who had been consulted had withdrawn upon learning that Harold continued to smoke. But a contributor to his respiratory failure was the lung lost to tuberculosis when he worked in the Army Medical Corps. If he had had two lungs—even emphysematous smoker's lungs—he would not now be facing death.

Harold could choose a "natural" death, which his lung specialist had

described to him as a progressive obtundation, longer and longer sleeping spells, and, at its best, a final sleep in which his brain simply would no longer be able to feel the oxygen lack, no longer muster the strength to take another inadequate, unsatisfactory breath. Or he could choose what some would call an "unnatural" death, by taking a pill that would make the next sleep just a tad too deep to allow his waning respiratory drive to continue. Until either of those events happened, he would spend each day waiting, wondering, parceling out each muscle flick, with its inevitable oxygen demand.

"The worst of it is the panic attacks," he told me. "I get a smothering feeling that I can't breathe—and I can't. I struggle to breathe, and my brain feels like it's drowning. I have medicine I can take for the attacks, but I can't control them."

Harold was fully plugged in with hospice visitors, and he appreciated their visits. At the very least, they broke up his social isolation. Beyond that, there wasn't much that could be done for him. He was permanently tied to an oxygen tank; he knew every drug, every treatment, every side effect. He simply needed more oxygen and less carbon dioxide in his blood.

"I don't know whether I'm really going to do it," he said, referring to taking the lethal dose. "Some days I think not and some days I think I want to. More of those lately, as I get weaker. But I really want the choice. When it gets most horrible, I can't stand the thought that it could go on forever that way. If I had the medicine here, I wouldn't get so panicked. I could take the bad times better because I'd know I wouldn't have to. I could stop it if I wanted." I recognized his logic from my work with patients suffering from panic attacks. Sometimes just carrying panic extinguishing pills in a pocket is enough.

"I want Harold with me for as long as possible," his wife said. "But he's the one who has to suffer, and I don't want him to suffer any more than necessary." She held out a photograph of a handsome, vigorous man with 50 pounds more muscle than Harold has. "This is what my Harold looked like when he was healthy," she added.

Harold's biggest fear is that, if his death is listed as a suicide, his wife will lose all her veteran's widow benefits. Otherwise, money plays no part in his decision.

I leave the house with my mind running through a list of doctors who owe me a favor and may be willing to do the necessary house call to complete a consultation. I keep thinking that Harold won't go through with it; he just wants the choice, the control. Months later, I learn, Harold did indeed take the medication, after he had developed massive edema and felt uncomfortable beyond relief.

### Not Going Gentle

Minnie is a legend among those who know her. Her husband's retirement is a liberating event. Now they can indulge her life's passion: travel. While they have their health, Minnie, the spark plug, uses her sharp wit and intrepid attitude to intimidate anyone who dares to present obstacles as they travel the world. They tour Europe and Asia, returning to Eugene only to check in with their children and grandchildren for life events and holidays. And while at home, Minnie invigorates friends and neighbors with her accounts of their travels and, most importantly, her attitude toward life.

I hear about Minnie weeks before I am approached to act as consultant. My



healthy, and maybe not even now. I can imagine her chuckling I can," she'd say. "I'm not done yet."

wife's coworker keeps talking about a neighbor, a fantastic elderly woman who is near death but whose mind and attitude are as sharp as ever. Her body is racked and dying, yet her mind and spirit are untouched by the process. If she could, Minnie would have her deathbed rolled onto a tour ship.

I read Minnie's chart. Her colon cancer has spread to her liver, and she is put through the usual rounds of chemotherapy, which do induce remissions and buy time. But finally she has reached the stage in which further chemotherapy is considered useless. The damage to her body will be greater than the damage to the cancer.

Minnie does the equivalent of a wartime fighting unit overrun by the enemy: she calls the bombs in on herself. She insists on another round of chemotherapy. Minnie is someone I would not have wanted to cross when she was healthy, and maybe not even now. I can imagine her chuckling to herself about the cancer cells. "I'll get those suckers any way I can," she'd say. "I'm not done yet."

Minnie lives up to her advance billing. In a somber house, alone with her husband, her body a bony, jaundiced squiggle lying on its side in her bed, her belly bloated with liver cancer and fluid beyond the swelling of pregnancy, she reveals her wit.

"This process is boring me to death!"

"Are you in any pain?"

"Not really. I'm uncomfortable, this belly. It's the weakness, and the nausea, but I've got pills for that. The worst of it is just having to lie here and watch this happen to me. And there's nothing I can do about it. I mean it: this is boring."

"I don't want to die," she adds. "I want to see my grandchildren grow up. I want to travel, see the world, meet people, live life. But if I can't do that, then heck, I've got no use for this process."

Her hospice worker has come and gone for the day. Her husband is now

functioning as Minnie's arms and legs, fetching for her, waiting on her.

Minnie's mental competency is not in question, but depression could still be an issue. I ask her husband whether her feelings about a planned death have changed or are out of character.

"No."

"Has there been a dramatic change in her outlook on this issue in the last few weeks or months?"

"No. Hell, she's always talked like this."

There really wasn't too much more to say, not as a consultant. Another doctor would actually prescribe the medicine. But Minnie liked having an audience, and it seemed to be a relief to her to have someone she could talk to about this now-all-consuming matter, so I stayed far longer than needed.

I was struck at the contrast between this scene, her isolation—even with her family members, friends, neighbors, and hospice workers—and the lofty, all-knowing, public and congressional debate on this matter. Where was even one of those senators or congressmen now, to explain to Minnie how and why it was necessary, in these final hours of her life, to die *their* way, as opposed to *her* way; to explain to Minnie what a great relief it would be to the living that the decision had been left to *their* God rather than hers.

Fate had dealt Minnie a card she couldn't control, and death was hovering. She had only two choices: to end her life, or to prolong her suffering in the belief that it would serve some purpose—perhaps God's plan, which, had she that faith, might make perfect sense. In the absence of such faith, though, it made little sense to her, and thus made her suffering seem all the more acute and pointless. Minnie, I knew, had no struggle with her faith. The uncertainty about the plan had to lie with those who would insist that she give up her need to control and submit meekly to their way.

"One thing, Minnie," I said. "You are so weak now, and you are very dehydrated and getting more so every hour. I would guess at this rate, within a day you will lapse into a sleep and then a coma and, without feeling or experiencing a thing, you will die naturally. Your fourteen-day wait before you get the medicine won't be up for another four days. You don't have to do this. In fact, I don't think you will get to do this unless you solve the dehydration problem."

Minnie thought about this, her brain like molecules in Brownian motion bouncing inside the walls of her skull. She then began the long, laborious, exhausting process against gravity, nature, and fate, human will against dying body, to lift herself to a sitting position. Suddenly she had a goal, a purpose.

"Fred, would you bring me a glass of water?"

And to me, "I'll get this water down and keep it down somehow. Thanks, Doc!"

So many questions and issues emerge from these experiences that never seem to be expressed in the legal and congressional debates. Clearly, control—not pain—is the issue: whether individuals have the right to control the method of their dying, or whether the government has the right to demand that the control be wrested away for some greater purpose. These patients are not worried about political wrangling over the Death with Dignity Act; in the process of dying, they are simply clinging to what little vestiges of control their fate has left them.

Minnie rallied her remaining strength, prolonged her consciousness and life to acquire the medication, and then, her position overrun by invaders, called in the ultimate chemical bomb. Get them suckers! ■

Peter M. Patricelli '71 is a physician with McKenzie Family Practice in Springfield, Oregon.

THE CONNECTION BETWEEN

# Mind & Body

WALTER CANNON, A PIONEER IN physiological research, liked to recount a story about voodoo death, or the power of taboo among the Maori of New Zealand. A young man visiting an older friend's home was served wild hen, which the

younger generations were prohibited from eating. The young man ate the meal, because he was assured that it did not contain wild hen.

Several years later, the older man asked the younger if he would eat wild hen. The young man replied that he would never violate the taboo. The elder laughed and confessed that he had once tricked him into eating the hen. The younger man grew terrified and began to experience physical distress. Within 24 hours, he was dead.

A taboo, Cannon concluded, could produce "a fatal power of the imagination working through unmitigated terror." Stirred by such stories,

An unbroken chain of HMS teachers and students have believed that medicine must respect the link between the mental and the physical

by EUGENE I. TAYLOR





**OLIVER WENDELL HOLMES**  
thought science should not  
replace the physician's  
proper focus in medicine—  
the patient.

# Holmes grumbled that the overemphasis on pure science in his own

Cannon joined a lineage of Harvard physicians who have pondered the connection between mind and body. From Oliver Wendell Holmes's championing of old women's folk remedies, to William James's investigations into hypnosis, to Herbert Benson's discovery of the relaxation response, an unbroken chain of teachers and students have believed that medical practice must take into account the inextricable link between the mental and the physical.

## Thumps and Doubts and Guesses

Mind/body medicine at Harvard can be traced at least as far back as Oliver Wendell Holmes, Class of 1836, who served as the Parkman Professor of Anatomy and Physiology at HMS from 1847 to 1882. Holmes earned

wide recognition for his work on puerperal childhood fever, especially his controversial theory that physicians bore responsibility for the high mortality rate among infants because they moved directly from the autopsy room to the birth chamber without washing their hands or changing their clothes.

Beyond his involvement in medicine, Boston's "beloved physician" was also a man of letters. He suffered, he once said, from the lifelong disease called *Cacoethes scribendi*, the "itch to write," and he defined "lead poisoning" as the disease that afflicts every good writer once the mind makes contact with printer's type. Holmes combined his literary and scientific skills to communicate the mind/body connection to younger physicians, ultimately championing

the notion of physician as naturalist, even as medicine was veering toward the microscopic, the chemical, and the quantitative.

Holmes believed that the world of ideas, feelings, and beliefs could have real effects on the body. "So long as the body is affected through the mind," he said, "no audacious device, even of the most manifest dishonest character, can fail of producing occasional good to those who yielded an implicit or even a partial faith." Holmes also acknowledged that unconscious factors may shape our actions. "A man who has paid twenty-five dollars for his whistle," he said, "is apt to blow it longer and louder than other people."

The most important contribution Holmes made to understanding the mind/body connection, however, was

## A LONG AND RICH TRADITION



**OLIVER WENDELL HOLMES**  
used his scientific and literary skills to communicate the links between mind and body

1836

1869

**WILLIAM JAMES**  
was the first of Harvard to contribute directly to the experimental analysis of the mind/body problem



**WALTER CANNON**  
chose to focus on the scientific study of emotions when studies of the cerebral cortex prevailed

1900



time was already interfering with the doctor/patient relationship.

the humanity he brought to the practice of medicine. He stood solidly against quackery, but believed that an old woman who knows how to make and apply a poultice is a better healer than the celebrated pathologist who "explores and thumps and doubts and guesses, and tells his patient he will be better tomorrow and so goes home to thumb his books over and make out a diagnosis."

Holmes also grumbled that the overemphasis on pure science in his own time was already interfering with the doctor/patient relationship. His critics branded him as backward and anti-scientific, yet his contention was that science should never replace the physician's proper focus in medicine—the patient—for it is in the context of the doctor/patient relationship that healing takes place.

### Mind Over Matter

Direct heir to the medical legacy of Holmes—as well as the transcendentalist literary heritage of Holmes and Ralph Waldo Emerson—was William James, Class of 1869. Although James was the first at Harvard to cross disciplinary boundaries between physiology and philosophy and to contribute directly to the experimental analysis of the mind/body connection, he did not act alone.

Among his HMS classmates were Henry Pickering Bowditch and James Jackson Putnam. Bowditch founded the first laboratory of experimental physiology in the United States, located on the third floor of the Medical School, which was then directly across from Massachusetts General Hospital. There, the three of them

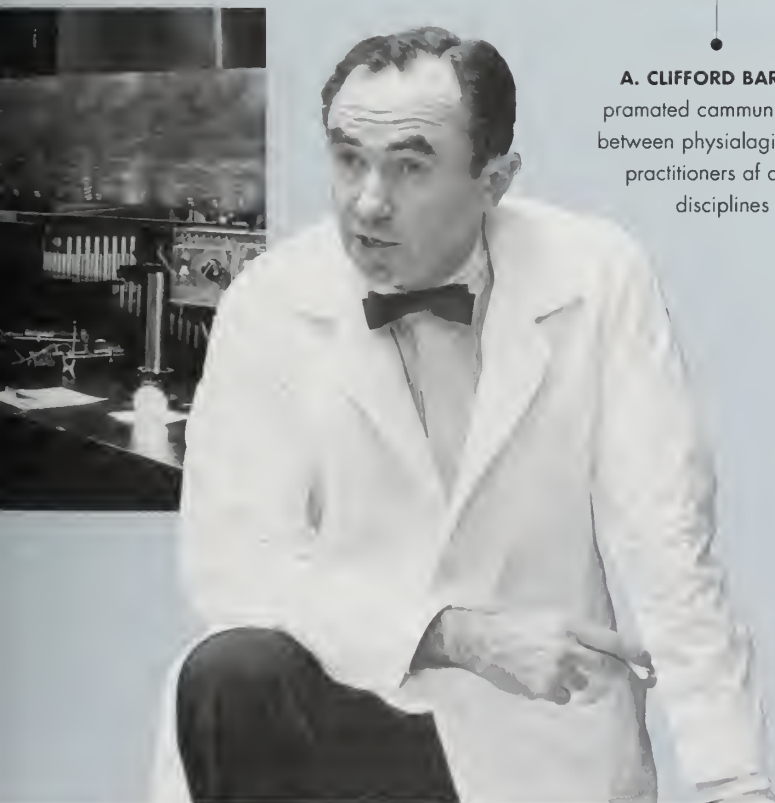
worked on pioneering experiments in brain neuropathology. Eventually Putnam went on to found the neuropathology laboratory at Harvard, and James started the University's first laboratory devoted to experimental psychology.

The three colleagues held dramatically different views on mental science, however. Putnam and Bowditch embraced the German idea that laboratory investigation is the only pure science; all else is applied. James acknowledged the importance of the German contributions to mental science, yet proceeded to conduct a series of investigations transmuting into psychology the techniques of French experimental physiology, which emphasized *la clinique*, or bedside teaching. The result was a new field that came to be known as experimen-

1943

#### **A. CLIFFORD BARGER**

promoted communication between physiologists and practitioners of other disciplines



#### **HERBERT BENSON**

coined the phrase "relaxation response" and helped found the field of biofeedback

1961

# James investigated the offbeat phenomena that had fascinated him for

tal psychopathology, which James offered as a graduate course at Harvard. There he taught students hypnosis, automatic writing, and other means of dissociating consciousness in order to artificially reproduce the symptoms of functional disorders of the nervous system, such as hysteria and neurasthenia. Consciousness, for James, was a biological fact with evolutionary consequences. Through conscious choices, the mind exerts an influence over the body, while the state of mind is influenced moment to moment by a host of unconscious physical conditions.

Particularly during the 1890s, James also investigated the offbeat phenomena that had fascinated him for most of his professional life, such as clairvoyance, telepathy, mediumship, and religiously induced states of consciousness. He believed that many lay mental healers were already ahead of medical science in understanding the mind/body connection; their methods were simply intuitive and unsystematic. At one point, he even mounted a vigorous defense of spiritualists and mental healers, believing that instead of trying to regulate them out of existence, the state legislature should solicit medical science to verify or disprove their claims.

James's own studies had hinted that ideas could be implanted in a highly suggestible subject—usually a Harvard student—that could cause paralysis, contractures, fainting, choking and, in rare cases, even bleeding. He also demonstrated that these effects could be instantaneously reversed through suggestion; a thought could create—or banish—a physical symptom. It was precisely James's innovative acceptance of such ideas that attracted a younger generation of HMS students, particularly Walter Cannon.

## The Fight-or-Flight Response

Walter Cannon, Class of 1900, originally a shy and retiring boy from rural Wisconsin, rose to become the

Higginson Professor of Physiology at Harvard and one of the preeminent figures in medical science in the twentieth century. He chose to focus on the experimental study of emotions in an era in which studies of the cerebral cortex prevailed, and through this work brought the mind/body problem furthest into the arena of an exact science.

As an undergraduate, Cannon fell under the influence of William James, whose theory of emotion, by then paired with the work of Danish investigator Walter Lange, was just then attracting international attention. The James-Lange theory was hotly debated following the publication of James's *Principles of Psychology* in 1890, and to help him respond to his critics, James assigned Cannon the job of scouring the scientific literature for all new work on emotion. The result was a detailed undergraduate essay that steered Cannon on a lifelong scientific quest to understand the digestive, the autonomic, and the affective physiology of humans.

Fascinated by the psychological cases that James had gathered to illustrate his ideas, Cannon began to seek historical, religious, and anthropological sources for additional examples of the ability of people under stress to perform extraordinary feats of strength and endurance. He even called on a neighbor who had served with General Custer for a firsthand account of the psychological methods both the Army and the Indians had used to prepare for battle.

Cannon's most enduring legacy to medical science was undoubtedly his notion of the fight-or-flight response—his recognition that the body reacts to stress and danger by creating a heightened chemical environment that is mobilized for action. He also conducted pioneering research into the neurohumoral basis of emotion, which occupied him into the late 1920s, after which he turned his attention to what we would today call the chemical mediation of nerve impulses at the synapse.

Cannon is also remembered for his investigation of unusual phenomena associated with the mind/body connection. In addition to his studies with Walter Alvarez on voodoo death, Cannon took a cue from James and gave lectures to medical students on hypnosis and suggestion. Later in life, he tried to summarize his physiological work within the larger context of sociology, looking at physiology both systematically and holistically. This approach was again partly attributable to the influence of James, who had steered Cannon away from philosophy and toward medicine. Cannon never abandoned his philosophical impulse, however, and continued to develop it on his own terms, pioneering in such concepts as physiological homeostasis.

## Carrying on the Tradition

The key figure who helped usher mind/body medicine at Harvard into the modern period was the late A. Clifford Barger '43A, the Robert Henry Pfeiffer Professor of Physiology. Born in Greenfield, Massachusetts, he graduated from Harvard College and HMS before interning at Peter Bent Brigham Hospital. He joined the Army, where, after basic training as a lieutenant, he conducted medical research.

After the war, Barger returned to HMS, where he remained for the rest of his career. Mild-mannered and modest, he is remembered as a beloved professor who took a deep interest in the individual lives of his students. A distinguished mentorship award has even been named in his honor.

Carrying on in the tradition of Walter Cannon, Barger focused on problems of the cardiovascular system while at the same time promoting interdisciplinary communication between physiologists and practitioners of other disciplines. He became a leading figure in the pathophysiology of the cardiovascular system, the first to experimentally produce heart failure in animals, and the first to



most of his professional life, such as clairvoyance and telepathy.



**BEYOND THE GRAVE:**  
William James believed  
that the material and  
spirit worlds could com-  
municate. Here he joins  
Mrs. Walden in séance.

# Benson had noted that a patient's blood pressure always rose when

describe the physiology of congestive heart failure.

Like Cannon, Barger was a keen advocate of animal experimentation. He was part of a generation of scientists who promoted a whole animal physiology, in which physiology was the integrating science that provided physicians with a picture of the total functioning organism. As a spokesman for that view, with Saul Benison and Elin Wolfe, he authored a biography of Cannon.

Barger's era was soon overshadowed, however, by dramatic new developments in the brain sciences, which required a more complex, reductionistic, and compartmentalized definition of the field in a variety of new specialties. He lived to see physiology in the context of the whole organism significantly diminish as a subject in the medical curriculum. Meanwhile, he fired the imagination of numerous students who took his holistic view into new areas of

medicine. One of these students who would go on to distinguish himself in the field of mind/body medicine was Herbert Benson.

## The Relaxation Response

After interning in medicine and holding a fellowship at the Thorndike Memorial Laboratory at Boston City Hospital, Herbert Benson '61 returned to work under Barger in 1967, first as a fellow in physiology and then as an instructor in physiology and medicine at HMS.

Benson had noted in his own practice that a patient's blood pressure always rose when measured in the doctor's office, often leading to over-medication. He attributed this elevation to the effects of stress—not at that time a well-recognized concept in medicine, but a topic of considerable experimental interest to Barger.

Benson approached his former teacher for an explanation, and Barger brought him into a remarkable experimental collaboration with some students of psychologist B. F. Skinner in order to develop an animal model demonstrating the effects of stress on hypertension. Succeeding beyond his original expectations, Benson helped found the field of biofeedback and, in collaboration with Gary Schwartz and David Shapiro at Boston City Hospital, went on to develop a human model showing the connections between stress and hypertension.

In the midst of these investigations, Benson also began studying transcendental meditators, noting that they were able to achieve deep states of physiological relaxation that seemed exactly the opposite of Cannon's fight or-flight response. He named this effect "the relaxation response." Within the autonomic nervous system, he found, decreased sympathetic tone has a significant impact on stress related states, including hypertension, anxiety, various forms of pain, and mild to moderate forms of depression.



**WAX MUSEUM:** Beginning in the 1870s, William James relied on wax devices as teaching tools in the Harvard Psychological Laboratory.



measured in the doctor's office, often leading to overmedication.



**BELOVED PROFESSOR:** A. Clifford Borger fired the imagination of numerous students who imported his holistic view of medicine into their own chosen specialties. One student who distinguished himself in the mind/body medicine field was Herbert Benson.

The relaxation response also has been associated with the physiological state that accompanies other forms of meditation and repetitive prayer. Benson has suggested, in fact, that the induction of the relaxation response may be a generic first step in achieving the various contemplative states associated with the world's major religions.

Coincidentally, Benson conducted his experiments on the relaxation response on the very site of the fight-or-flight response experiments performed 50 years earlier, in rooms where Cannon's charts still adorned the walls. Today, Benson is the founding president of the Mind/Body Medical Institute at Beth Israel Deaconess Medical Center. Known internation-

ally, this program now has branches in hospitals and schools throughout the United States, and is an integral part of the Harvard University Health Services' progressive program in stress reduction.


### A Proliferation of Forms

Today, various forms of mind/body medicine are found throughout our medical culture. Specialties such as psychophysiology, psychosomatic medicine, consultation liaison psychiatry, and medical psychology are all practiced throughout Harvard's more than two dozen teaching hospitals. Social medicine and therapies from non-Western cultures represent addi-

tional developments in the medical sciences that capitalize on the mind/body connection.

Indeed, the University's more recent foray into the neurosciences—the Mind/Brain/Behavior Initiative—strives to foster interdisciplinary communication across the sciences in ways that produce entirely new and unforeseen consequences for the way science is conducted and patient care is delivered. These developments all have new names, but the ideas behind them have had a long and distinguished history at Harvard. ■

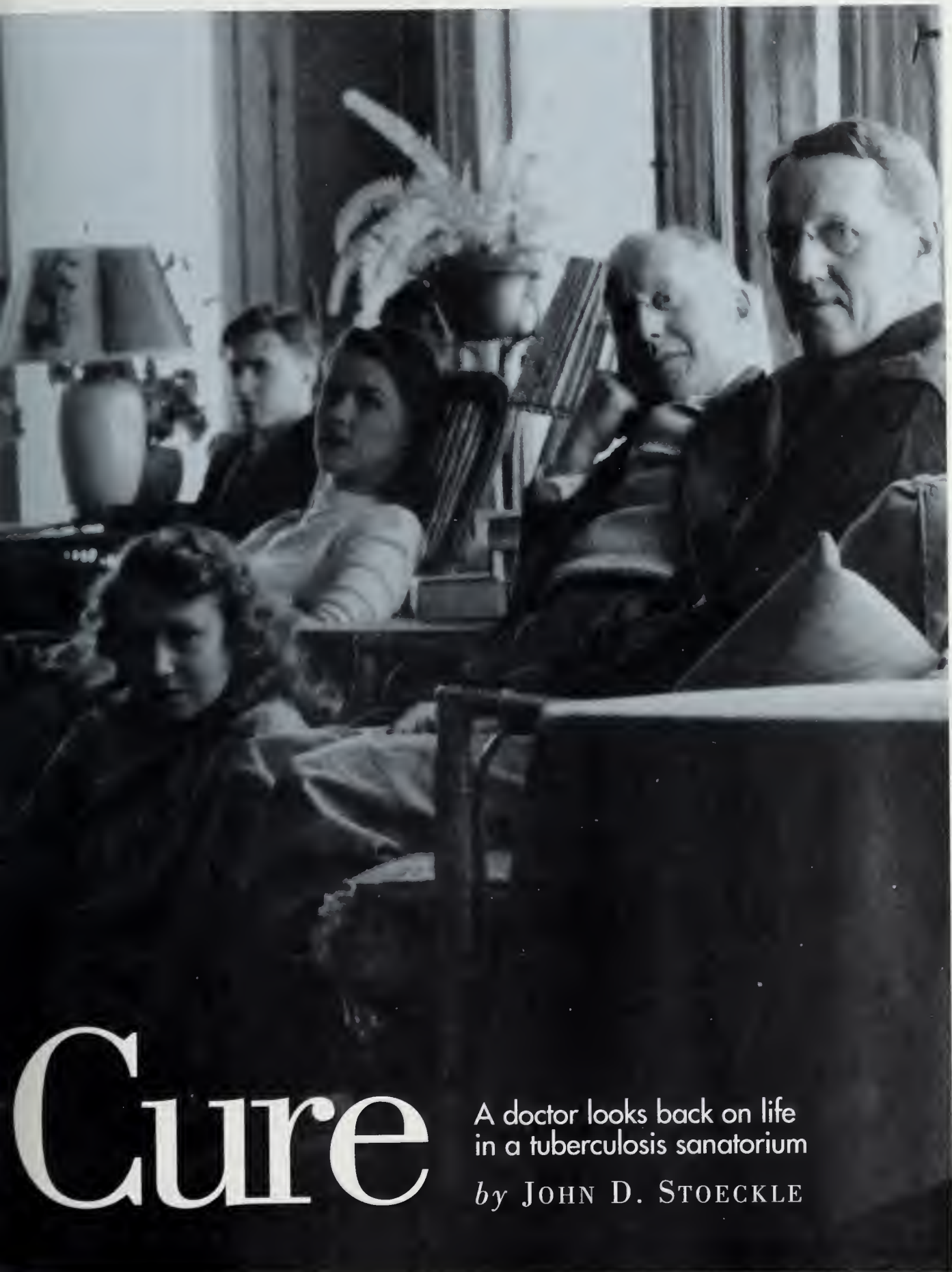
*Eugene I. Taylor, PhD, is a lecturer on psychiatry at HMS and a senior psychologist on the psychiatry service at Massachusetts General Hospital.*



IN THE SAN: The author, John Stoeckle (in back, second from left), poses with other patients at the Trudeau Sanatorium on Saranac Lake in the Adirondacks.

# Taking the





# Cure

A doctor looks back on life  
in a tuberculosis sanatorium

*by* JOHN D. STOECKLE

# W

hen I was diagnosed with tuberculosis during my third year at HMS, I was reassured that “many doctors get TB but get over it.” Indeed, in the 1940s, TB was almost an occupational hazard of hospital life, with our exposure coming from the wards, where patients with active, open cases were awaiting beds at the sanatoriums, and from autopsy rooms, where dissecting knives produced showers of acid-fast bacilli. Many health professionals up and down the East Coast—including medical students, residents, and nurses—contracted the disease and, although our exact numbers were never tabulated, they seemed great.

To recover, some infected health professionals headed north to Trudeau Sanatorium at Saranac Lake in the Adirondacks, while others went to county or state sans. Those who were in the service during World War II went to designated Army or Navy hospitals if on active duty, and to private sans or Veterans Administration hospitals if not. Some stayed home to receive collapse therapies from private physicians.

Upon my diagnosis, I was admitted to Peter Bent Brigham Hospital. After a week of bed rest, gastric cultures, chest films, and daily visits by the residents (quick and friendly, as I had done a rotation at that very hospital six months before), I was sent away to “take the cure.” I was admitted into

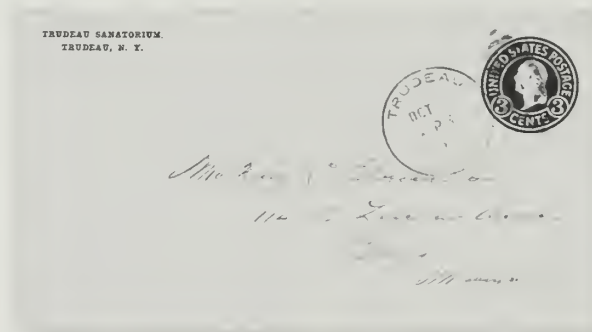
Trudeau Sanatorium with a diagnosis of minimally active TB. As I prepared to leave Boston and all that was familiar, I worried that I would be forgotten. The ward attending, Howie Armstrong, reassured me that I would not. “HMS will have a place for you when you get out,” he promised.

## Doctors as Patients

After an admission checkup by Frank Epstein (then a summer Yale extern, now the William Applebaum Professor of Medicine at HMS), I was assigned to bed rest at Kerbs 1, a cure

cottage inhabited by medical students, physicians, and medical researchers. We eight made up the “doctors’ cottage” (despite the presence of six non-

**STAYING  
IN TOUCH:**  
Correspondence with friends and family helped ease patients’ worries that they would be forgotten.







**INTO THE WOODS:**  
Kerbs 1 Cottage  
at the Trudeau  
Sanatorium  
became known  
as the "doctors'  
cottage."

physicians). Nurses who had been infected in various New York hospitals were clustered in cottages, too.

In fact, health professionals occupied 10 to 20 percent of Trudeau's 200 beds, and still more nurse and doctor "cures" were on the medical staff. "San doctors" were invariably cures who stayed on for clinical work and, sometimes, careers as chest physicians. Although they did not necessarily self-disclose their illness, the supervising physicians—Gordon Meade from Rochester and the late Roger Mitchell '34 from HMS—could be counted among the recent doctor cures. Secing them at work gave us hope that we too would be able to return to clinical life.

### Dread and Hope

In the early 1900s, sanatorium conditions had been grim. But in the 1940s, our experience was decidedly optimistic and, by contemporary standards, even luxurious. If TB was as it is today—a disease of

poverty—this was not reflected in life at Trudeau. The san was not only a rest retreat, but an environment and community in which to learn and grow, if, of course, our disease didn't relapse.

Although the diagnostic bad news that had landed us in the san initially made us afraid that we might die, our fears about having contracted a potentially fatal disease quickly relented. Our lack of symptoms, our newly converted tuberculin tests, and our chest films showing minimal infiltrate were signs that the disease had been caught early, which made us confident that our lives would be spared. And we knew that, even if our disease progressed, there was the promise of a ready cure with newly discovered streptomycin or one of the old collapse therapies.

More disturbing to most of us than the physical discomforts of our disease were the psychological consequences of our diagnosis. Although we were not visibly stigmatized by an illness that only appeared on chest films, many of us considered our-

If a

Depending on our chest films, we were prescribed bed rest in monthly doses. Then we all faced the wait and worry about what our follow-up x-rays might reveal—relapse, resolution, or arrest—and the opinion on when we could get out of bed, or even out of the san itself.

Many of our anxieties melted away, though, in the everyday life of the san, where everyone was infected and the diversions were plentiful. We were in bed morning, noon, and night, with music and news provided by the Montreal station. The library provided us with books—a chance to catch up on some of the Great Books left unread in college, or to live vicariously through the adventures of the characters in all those novels we had neglected in favor of medical texts. After an afternoon snooze, we would play bridge and solitaire. Winter was freezing, but electric blankets kept our beds warm. In fine weather, we often slept on the cottage porches, each of which had two beds.

But with improved or even stable chest films, our bed rest restrictions were gradually lifted and we could go to the main building for meals in the coed dining hall, where our long talks became group counseling, each of us with stories to tell. One gossip theme we never tired of was the unstable disease of others. Continuing stability or x-ray improvement meant confident pride in our rested bodies and opportunities for increased activity.

In the winter, we could stroll the campus or even take a taxi to the lounge-bar downtown to eat, drink

△ 335-5

## THE PRICE OF HEALTH:



to the infirmary, where bed rest was strict, more tests were done, collapse therapies, which meant longer, more uncertain stays.

beer, and dance to the jukebox. In the summer, we would motorboat to Ecstasy Island on Lower Saranac Lake, for picnics and swims. These outings often provided opportunities for "cousining," a euphemism for often illicit liaisons, sometimes between the single and married and even between nurses and patients.

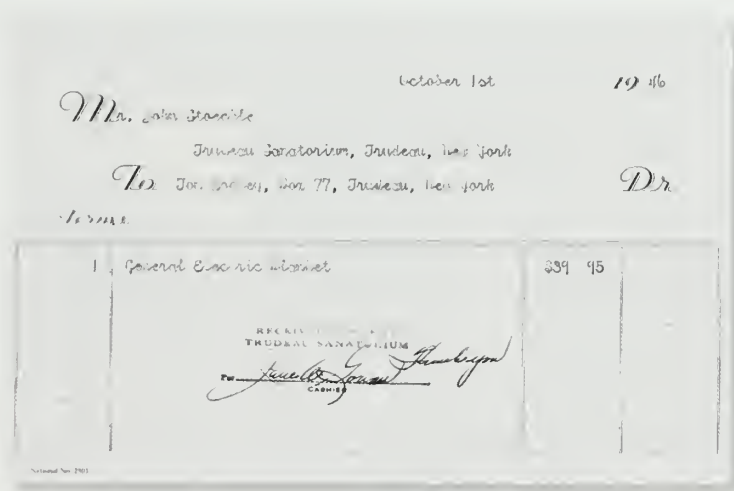
In addition to the social life associated with taking the cure were clinical opportunities to learn about TB and its treatment. When our cases arrested, we might be chosen to join the medical staff as student externs. Our clinical experience might include helping take care of sicker patients in the infirmary; giving supervised pneumoperitoneum and pneumothorax collapse therapies; reading x-rays; doing lung function testing; observing thoracoplasties, phrenic nerve compression, and bronchoscopies at Saranac Lake Hospital; and visiting nearby sans. Caring for fellow patients who were worsening gave us a powerful reminder that not everyone recovered from TB.

### Then and Now

When I returned to HMS in 1947 after 15 months away, my experiences of illness and of clinical work remained with me even as TB itself seemed to fade from clinical and public health practice. Trudeau closed in 1954, as did public and private sanatoriums around the country. With the advent of new TB drugs, treatment became an outpatient service.

That old cure of isolation, rest, and open air was abandoned, with its prescriptive bed rest decried as misused, harmful, unproven, unnecessary, and—in today's health care market—far too costly. Such long-term retreats for healing are no longer used. In the history of a disease that has spanned centuries and killed perhaps more people than any other infectious disease, our cure seems like an anomaly.

Today, people with TB are treated at home or on the street, where urban air differs markedly from those mountain breezes, rest is not an option, and the support offered by a community of infected peers no longer exists. For patients today, so much of that old common experience of illness is missing. Without any institutional group life for the cure, a vast unconnected population of tuberculars take their pills all alone.



In fact, only one in five people now infected with TB receives adequate treatment. To control and cure this devastating worldwide epidemic, the World Health Organization has adopted the treatment strategy of directly observed therapy, short course (DOTS), which relies on fast, economical smear tests for diagnosis, followed by a six-month regimen of standard drugs. Yet the new resistant strains require a different tactic. In the face of epidemics of multidrug-resistant TB, Paul Farmer '90 and Jim Young Kim '91, co-directors of the Program in Infectious Disease and Social Change at HMS, have joined with the World Health Organization in advocating DOTS Plus, which involves a combination of longer individualized therapy and daily health worker home visits.

Each year, more than two million people die from TB, and another eight million develop it. TB is again seen as a disease of poverty, devastating communities in developing countries and inner cities. These alarming trends make our life at Trudeau seem, in retrospect, more like a stay at a middle-class country club than a medical regimen. With multidrug-resistant TB on the rise, even more generations are becoming vulnerable to this persistent killer. Ironically, our modern treatments are providing us with dangerous new variations of the same old germ. ■

John D. Stoeckle '47 is HMS professor of medicine emeritus and a physician at Massachusetts General Hospital.

**WARM-UPS:**  
On cold winter nights, \$39.95 electric blankets heated the cottage beds.

# glorious DEEDS



Committed to  
relieving human  
suffering,  
philanthropist  
Henry Isaiah Dorr  
gave the anesthesia  
field an early  
boost

by JOHN P. BUNKER

IN 1910, HENRY ISAIAH DORR, A RETIRED physician and dentist, offered Harvard \$2,000 a year—the income from a \$63,000 gift—to establish an endowed chair devoted to research and teaching in anesthesia. President A. Lawrence Lowell was almost scornful in his reply. “I ought to say that \$2,000 is not as much as we pay for most full professorships even in the clinical departments, where a man gives a part only of his time to the school,” he wrote. “No doubt the word ‘chair’ would not necessarily mean a full professorship.”

Dorr was determined, however, and answered, “I would like the word ‘chair’ to mean a full professorship, the occupant of which to be a man of eminence.” By 1917, he was able to offer \$100,000, which was accepted, and the Henry Isaiah Dorr Chair in Research and Teaching in Anaesthesia and Anaesthetics was established, the first endowed

chair of anesthesia in the world. By the time of his death in 1927, Dorr had increased his bequest to \$200,000.

The bequest to Harvard was made, Dorr said, “for the benefit of the medical and dental students of Harvard College and suffering humanity.” Gifts to Temple University were similarly designated, and a final bequest to a society for the prevention of cruelty to animals was a donation to “poor, helpless, dumb animals for their protection and well-being.”

Dorr’s lifelong interest in anesthesia was a manifestation of his deep concern for suffering. He wrote, in his unpublished papers, “Of all the discoveries of value in medical science of the past, present, and—if I may be prophetic—future, none have or can excel that of anesthesia.” He quoted “an eminent teacher and surgeon” as saying, “The introduction of anesthesia in 1846 abolished, wiped out of exis-





An etching of William T. G. Martan, a Bastan dentist, conducting the first public demonstration of ether at Massachusetts General Hospital on October 16, 1846. John Collins Warren conducted the surgery, which was the removal of a tumor under the patient's jaw. The patient, Gilbert Abbott, declared that he had felt no pain during the operation and was discharged less than two months later.

tence at a step a sum total of human suffering so stupendous that the miseries of war, famines, and pestilences are as nothing in comparison."

To his compassion, Dorr added a reverence for science and an awareness of its cost. "Reflect upon the marvelous progress that has resulted from endowed Research Laboratories, made possible by praiseworthy men of wealth, and who study the public welfare in times to come," he wrote. "These are the men whose names and glorious deeds will be transmitted to posterity."

Dorr's respect for knowledge and appreciation for the value of money were those of a self-made man. He was born in 1844 in Ipswich, Massachusetts, into a family he described as "poor in worldly goods." His mother died "before his memory" and his father when Dorr was six. He was sent to live on the New Hampshire

farm of his father's widowed sister. Subjected to "extreme privation and cruelty" by his aunt's new husband, he fled at night by stage coach at the age of eight, "the commander-in-chief," he said, "of five red cents, earned honestly, however, by selling roasted chestnuts."

Dorr attended Harvard in 1869 and 1870, after three years of serving in the Union Army during the Civil War. He fought every engagement during those years, he said, and, although three horses were shot from under him, he was fortunate to "come through without a scratch." He was 16 years old when he first donned his blue uniform.

"I had to lie to get in," he said, "but they forced me to. A year before that, when I told them my right age, they would not have me. But it was a white lie, I think, for I prevaricated in order to serve my country. So I trust that the


little fib will not be counted against me. I did pay for it, though, for I virtually had to start my schooling all over again when I received my discharge, and it naturally set me back three years. But I don't regret it."

Elizabeth Snow Bissett, Dorr's great-niece, believed that his experiences in the war fired his resolve to go into medicine. "Whether Dorr's early and vivid memory of his emaciated father dying from a wasting disease turned his interest subconsciously towards medicine as a career, I can only conjecture upon," she wrote. "He believed from an early age that he possessed both the capabilities and tenacity to become 'an educated man.' His determination to train for a career in medicine, however, appears to date from his return from the Civil War at age 19, with three years of combat duty and with \$350 of army pay credited to his account."

“Of all the discoveries of value in medical science of the past, prophetic—future, none have or can excel that of anesthesia.”

Dorr's savings for his education grew so slowly that a prosperous dentist finally persuaded him to accept financial assistance, on the condition that Dorr abandon his plan to study medicine and take up dentistry instead. He enrolled as a dental student at Harvard and, following his graduation, practiced dentistry for several years. His ambition to become a physician was not realized until he was graduated from Jefferson Medical College at the age of 39.

In 1878, Dorr was appointed adjunct professor of practical dentistry at the Philadelphia Dental College (later to become the Temple University School of Dentistry) and was promoted to professor of clinical dentistry a year later. He introduced the teaching of anesthesia into the dental curriculum, writing in his unpublished notes that it was, as far as he knew, “the first systematic course of instruction in anesthetics and anesthesia.” In 1889, Dorr's appointment was changed to professor of the practice of dentistry, anesthesia, and anesthetics.

 **ALSO** IN HIS PERSONAL NOTES, Dorr described his use of nitrous oxide and oxygen anesthesia, adding an excerpt from a local newspaper column: “Many experiments have been made in the use of anaesthetics, but none has been so successful as the one which took place at the Philadelphia Dental College last Friday afternoon. This is the first operation with nitrous oxide gas in combination with oxygen for an anaesthetic in short surgical operations.

“The patients under this combination of gases,” the newspaper column continued, “do not exhibit the excitement or groaning as when under the influence of nitrous oxide or other administrations. The lips retain their usual color and the patients experience but little acceleration of the pulse. The duration of the anaesthetic is longer and the operation for the administration is quite simple. It is a very recent importation from England and as this is the first use of it in the United States, Philadelphia scientists have displayed a great amount of interest.”

Dorr was apparently unaware that Edmund Andrews had administered oxygen with nitrous oxide in Chicago 15 or 20 years earlier, in 1868. Nevertheless, it was an interesting and noteworthy accomplishment. What other scientific, medical, or dental contributions Dorr may have made are undocumented. His obituary in the Winchester, Massachusetts newspaper stated that he had authored several books on anesthesia, and a bronze plaque at the dental research laboratory he endowed at Temple University described him as “an ardent research worker.”

Dorr resigned from the faculty of the Philadelphia Dental College in 1896, apparently because of ill health. He suffered from “a kidney condition” and chronic asthma, and his physicians gave him only six months to live. His resignation was further precipitated by the college's proposal that each faculty member contribute \$5,000 to enable it to purchase land and erect a new building. Dorr cited his failing health as the reason he could not participate. Yet he survived his physicians' gloomy prognosis by 30 years.

In the years following his retirement, Dorr and his wife apparently

traveled a good deal, perhaps in search of relief from his asthma. It is not known whether he practiced medicine or dentistry. In 1914, Dorr and his wife moved to Massachusetts to live with a niece.

During the final years of his life, Dorr occupied himself primarily with his investments, by which he hoped to maximize his bequests. He was moderately successful: assets of approximately \$63,000 in 1910 appreciated to \$100,000 in 1917, and to \$265,000 at the time of his death ten years later. Dorr achieved this growth by investing in municipal and railroad bonds rather than stock, which he considered too risky. Although Harvard's administrators fretted under the constraints imposed by our “fussy and suspicious friend,” Dorr's caution was vindicated in the 1929 stock market crash, which his endowed funds survived without loss.

If Dorr was thrifty and shrewd in his financial activities, his purpose was solely to protect his bequests. He even took precautions to ensure that his wife could not interfere with his plans after his death. She was to receive all income derived from the estate “in accordance with her requirements and comfort, during her life.” If, however, she “should take against my will, I absolutely revoke all provisions made in her behalf and for her benefit.”

As it turned out, his innumerable cousins and more distant relatives did make an unsuccessful attempt to break the will, and Harvard tried to circumvent his plans as well. In 1919, long before Dorr's death, HMS Dean David Edsall solicited and obtained President Lowell's permission to use the Dorr Fund for pharmacology rather than for anesthesia, “a subject,” he wrote, “in which it really is unnec-



present, and—if I may be

—HENRY ISAIAH DORR

essary and undesirable to have a full professor and certainly undesirable to have an actual department.” But the funds would not become available for more than ten years.

Dorr died in 1927, his wife died two years later, and the estate was settled in 1930. By this time, the value of a research chair in anesthesia was recognized, largely due to the efforts of Edward Churchill, who had recently been appointed professor of surgery at Massachusetts General Hospital. Churchill saw the great potential value of an academic program in anesthesia, one that could direct attention and effort to the many important physiological and pharmacological problems he had encountered as a pioneer in thoracic surgery.

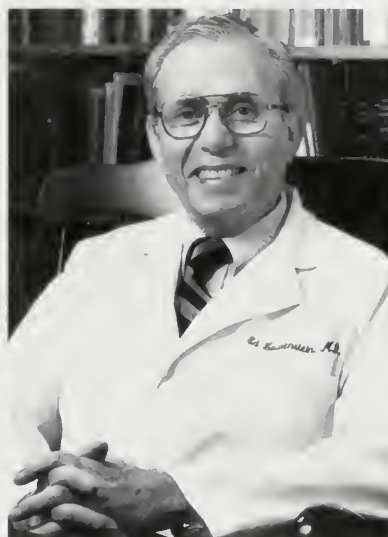
A search committee was convened in 1933, with Churchill as chairman. In 1936 the committee selected the late Henry K. Beecher '32, then a young surgical resident at Massachusetts General Hospital. In 1941, after a five-year probationary period, Beecher became the first Henry Isaiah Dorr Professor of Research and Teaching in Anaesthesia and Anaesthetics.

Dorr made his bequests to Temple University during the last two years of his life. As he had instructed, the funds were used to build a laboratory for research and teaching in oral pathology. The university urgently needed a laboratory and did not require much persuasion to implement Dorr's wishes. But, with typical determination to leave nothing to chance, Dorr added the provision that “if the University should refuse to establish the advance course of study as above provided...the principal and income shall be given to Harvard University.”

Today, Henry Isaiah Dorr is remembered as little more than a

name, the donor of an endowed chair in anesthesia at Harvard and of a research laboratory at Temple that has long since disappeared, along with the building in which it was housed. Yet Dorr was a great deal more than a name: he was a prophet who combined natural compassion and Yankee shrewdness with a reverence for science and a vision of the academic practice of anesthesia that was years ahead of his time. Today, he would take great pleasure to find that, in his own words, his “glorious deeds” have indeed been “transmitted to posterity” in the Anaesthesia Research Laboratory at Massachusetts General Hospital. ■

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**MEN OF EMINENCE:** Three physicians have held the title of Henry Isaiah Dorr Professor of Research and Teaching in Anaesthesia and Anaesthetics: Henry K. Beecher (top), Richard J. Kitz (center), and Edward Lowenstein (bottom), the current holder.

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